(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
3 August 2006 (03.08.2006)

PCT

(10) International Publication Number
WO 2006/081327 A2

(51) International Patent Classification:
A61K 31/58 (2006.01) *A61K 31/517* (2006.01)
A61K 31/5513 (2006.01) *A61K 31/47* (2006.01)
A61K 31/551 (2006.01) *A61K 31/445* (2006.01)
A61K 31/55 (2006.01) *A61K 31/44* (2006.01)

(21) International Application Number:
PCT/US2006/002711

(22) International Filing Date: 25 January 2006 (25.01.2006)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/646,967 25 January 2005 (25.01.2005) US

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(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *without international search report and to be republished upon receipt of that report*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 2006/081327 A2

(54) Title: SMALL MOLECULES THAT REDUCE FUNGAL GROWTH

(57) Abstract: The present invention relates to methods for reducing the growth of a fungus with an anti-fungal small molecule. Methods for reducing fungal cell growth in a subject with an anti-fungal small molecule and related compositions are provided. Topical lotion formulations of an anti-fungal small molecule and a topical carrier are also provided.

SMALL MOLECULES THAT REDUCE FUNGAL GROWTH

Related Applications

This application claims priority to US Provisional Application No. 60/646,967, filed January 25, 2005, the entire contents of which are herein incorporated by reference.

Field of the Invention

Methods for reducing the growth of a fungus with an anti-fungal small molecule are provided. Methods for treating fungal infection in a subject with an anti-fungal small molecule and related compositions are also provided. Compositions for reducing the growth of a fungus are provided. Topical lotion formulations of an anti-fungal small molecule and a topical carrier are also provided.

Background of the Invention

The invention is based on the discovery that anti-fungal small molecules can reduce the growth of a fungus. These anti-fungal small molecules can be used to treat a fungal infection, such as that caused by *Candida albicans*. *C. albicans* is the most common and arguably the most important causative agent of human fungal infections (Edmond, M.B. et al., 1999, Clin. Infect. Dis., 29:239-244). The yeast-to-hyphal morphological transition is essential for the virulence of *C. albicans*. It is a major opportunistic pathogen of immunocompromised hosts, including AIDS patients and those undergoing chemotherapy, tissue transplants or with central venous catheters. Studies indicate that up to 90% of AIDS patients suffer from oropharyngeal and esophageal candidiasis, in which *C. albicans* is the major causative agent (Schmidt-Westhausen, A. et al., 1991, J. Oral Pathol. Med., 20:467-472). Identification of novel anti-fungal targets is especially difficult as fungi are eukaryotic microbes that share many common cellular components with mammalian cells. Therefore, understanding processes unique to fungi, such as the yeast-to-hyphal transition, will undoubtedly lead to tremendous insight into virulence mechanisms and may ultimately lead to new anti-fungal therapeutic targets and drugs.

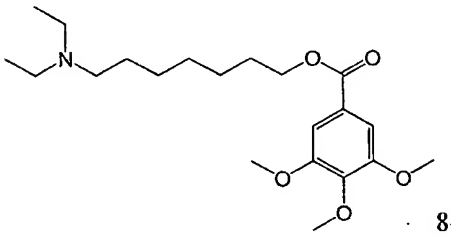
The need for new anti-fungal therapeutics is especially critical since there are serious side effects due to renal and liver dysfunction associated with the polyenes (*i.e.*, amphotericin B, nystatin) that are usually used to treat *C. albicans* infections. In addition, a significant increase in resistance to the less toxic azole drugs (*i.e.*, fluconoazole) has occurred within the patient population, especially HIV-positive patients.

Summary of the Invention

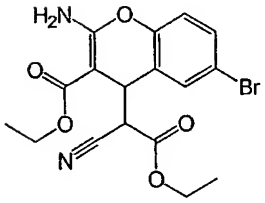
The invention provides in one aspect a method for reducing the growth of a fungus by contacting a cell with an anti-fungal small molecule in an amount effective to reduce the growth of a fungus. The invention also provides methods for treating a fungal infection in a subject by administering to a subject in need thereof an anti-fungal small molecule in an amount effective to reduce the growth of a fungus. Compositions for reducing the growth of a fungus are also provided. The compositions comprise an anti-fungal small molecule and an anti-fungal agent. Topical lotions are provided that comprise an anti-fungal small molecule and a topical carrier.

In an aspect of the invention a method for reducing fungal growth of a fungus by contacting a cell with an anti-fungal small molecule in an amount effective to reduce the growth of the fungal cell are provided.

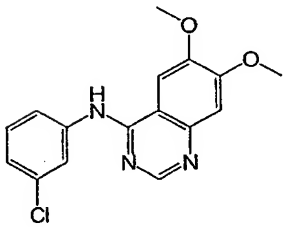
In one aspect of the invention anti-fungal small molecules, analogs and salts thereof are provided. In one embodiment of the invention the anti-fungal small molecules have the following structures:



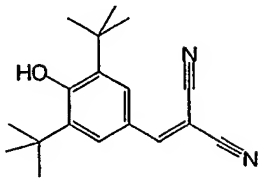
8-(N,N-Diethylamino)-octyl-3,4,5-trimethoxybenzoate, HCl (TMB-8)



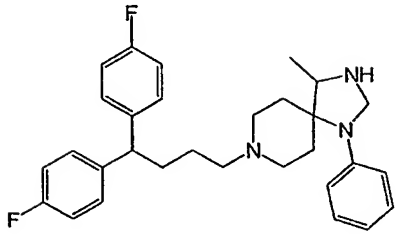
Ethyl [2-amino-6-bromo-4-(1-cyano-2-ethoxy-2-oxoethyl)]-4H-chromene-3-carboxylate (HA14-1)



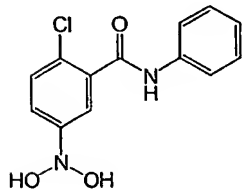
N-(3-Chlorophenyl)-6,7-dimethoxy-4-quinazolinamine (Tyrphostin AG1478)



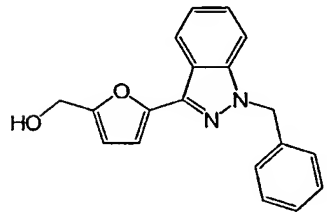
[[3,5-bis(1,1-Dimethylethyl)-4-hydroxyphenyl]methylene] propanedinitrile (Tyrphostin 9)



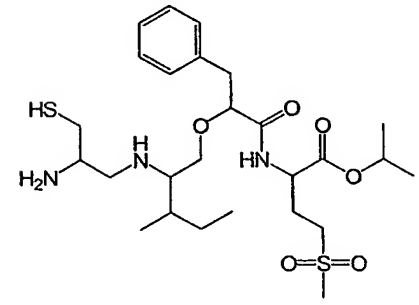
8-[4,4-bis(p-Fluorophenyl)butyl]-1-phenyl-1,3,8-triazino[4.5]decan-4-one (Fluspirilene)



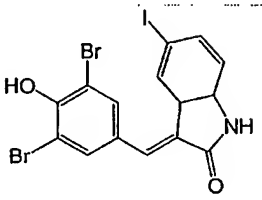
2-Chloro-5-nitro-N-phenylbenzamide (GW-9662)



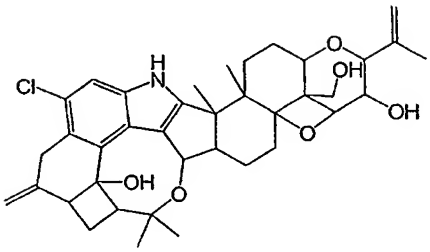
3-(5'-Hydroxymethyl-2'-furyl)-1-benzylindazole (YC-1).



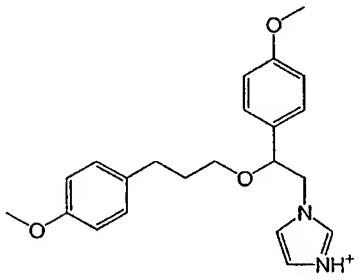
(2S)-2-[[(2S)-2-[(2S,3S)-2-[(2R)-2-Amino-3-mercaptopropyl]amino]-3-methylpentyl]oxy]-1-oxo-3-phenylpropyl]amino]-4-(methylsulfonyl)-butanoic Acid 1-Methylethyl Ester (L-744,832)



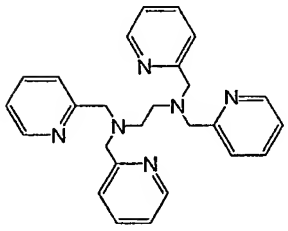
3-(3,5-Dibromo-4-hydroxybenzyliden)-5-iodo-1,2-dihydroindol-2-one (GW5074)



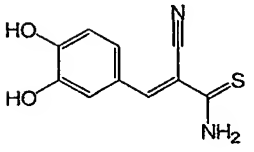
Penicillium palitans Penitrem A



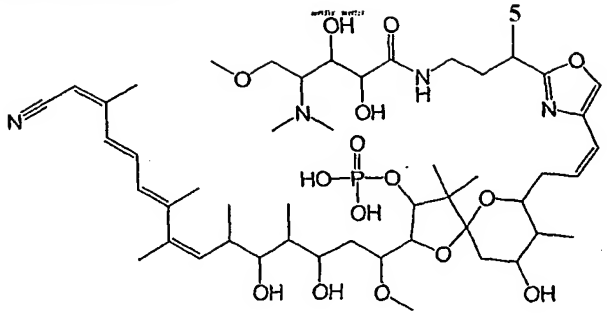
1-[β-[3-(4-Methoxyphenyl)propoxy]-4-methoxyphenethyl]-1H-imidazole, HCl (SKF-96365)



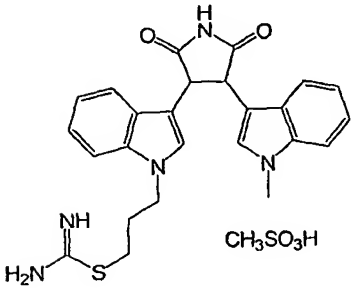
N,N,N',N'-*tetrakis*-(2-pyridylmethyl)-ethylenediamine (TPEN)



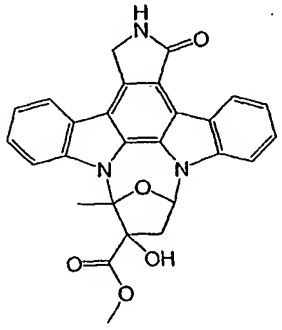
3,4-Dihydroxy-a-cyanothiocinnamamide, a-Cyano-3,4-dihydroxythiocinnamamide (Tyrphostin 47, AG213)



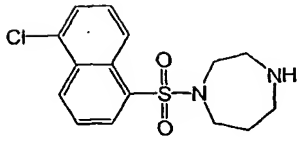
Discodermia calyx Calyculin A



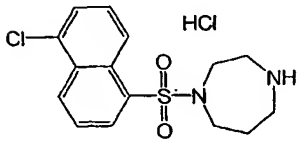
3-[1-[3-(Amidinothio)propyl-1H-indol-3-yl]-3-(1-methyl-1H-indol-3-yl)maleimide Bisindolylmaleimide IX, Methanesulfonate (Ro 31-8220)



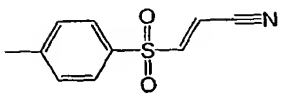
Cell permeable protein kinase inhibitor from Nocardiopsis (K252)



1-(5-Iodonapthalene-1-sulfonyl)homopiperazine (ML-7)

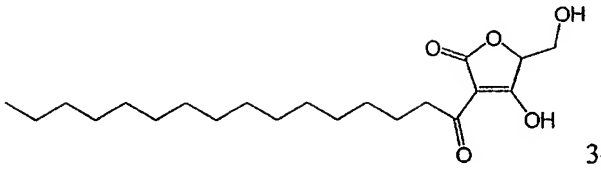


1-(5-Chloronapthalene-1-sulfonyl)homopiperazine, HCl (ML-9)

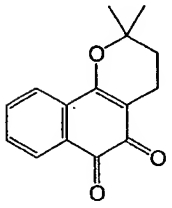


(E)3-[(4-Methylphenyl)sulfonyl]-2-propenenitrile

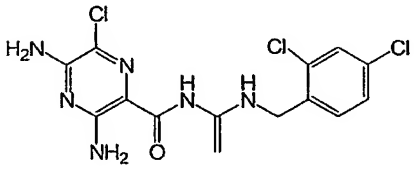
(BAY 11-7082)



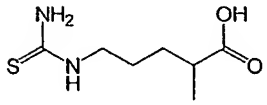
3-Hexadecanoyl-5-hydroxymethyl-tetronic Acid (RK-682)



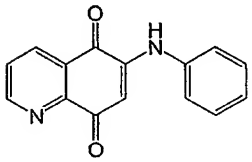
Tabebuia avellanedae β-lapachone



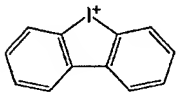
2,4-Dichlorobenzamil



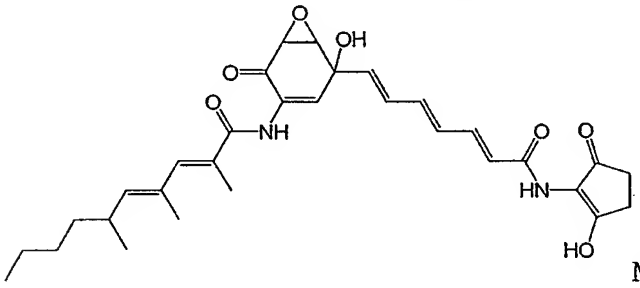
2-Thioureido-L-norvaline (Thiocitrulline)



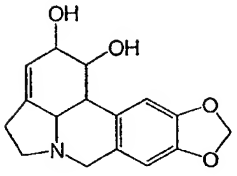
6-Anilino-5,8-quinolinequinone (LY-83583)



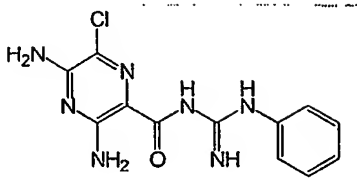
Diphenyleneiodonium



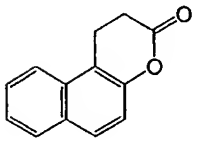
Manumycin A inhibitor of ras farnesyltransferase



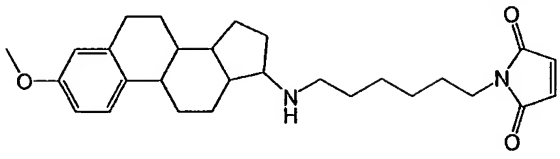
Lycorine



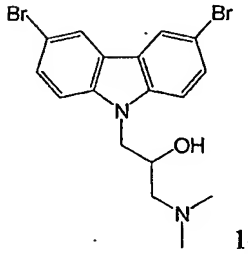
3,5-Diamino-6-chloro-N-[imino(phenylamino)methyl] pyrazinecarboxamide (Phenamil)



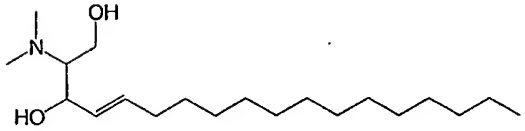
1,2-Dihydro-3H-naphtho[2,1-b]pyran-3-one (Splitomycin)



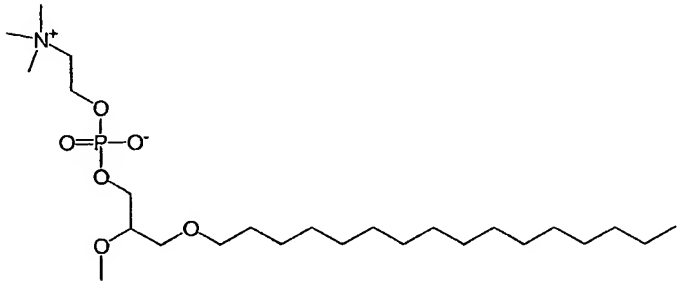
1-(6-(17β-3-methoxyestra-1,3,5(10)-trien-17-yl)amino)hexyl)-1H-pyrrole-2,5-dione (U73122)



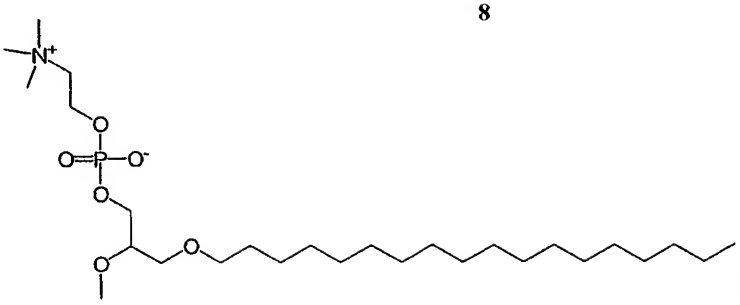
1-(3,6-Dibromocarbazol-9-yl)-3-dimethylaminopropan-2-ol (Wiskostatin)



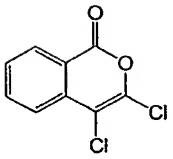
N,N-dimethylsphingosine



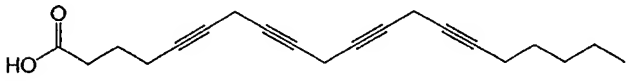
1-hexadecyl-2-methylglycero-3-phosphatidylcholine



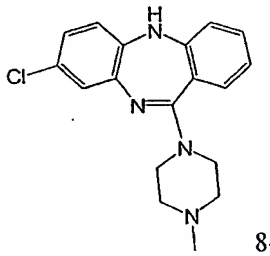
1-octadecyl-2-methylglycero-3 phosphatidylcholine



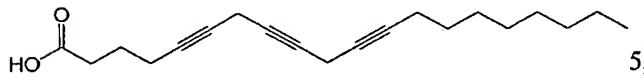
3,4-dichloroisocoumarin



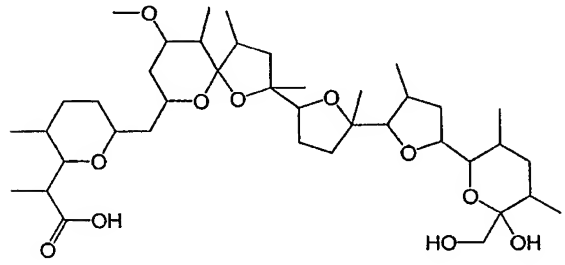
5,8,11,14-eicosatetrayonic acid



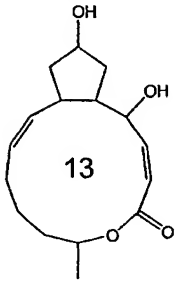
8-Chloro-11-(4-methyl-1-piperazinyl)-5H-dibenzo[b,e][1,4]-diazepine (Clozapine)



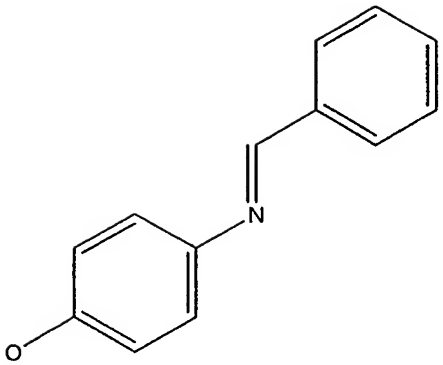
5,8,11-eicosatetrayonic acid



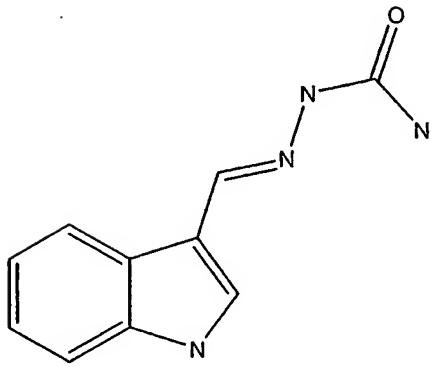
Streptomyces hygroscopicus (Nigericin)

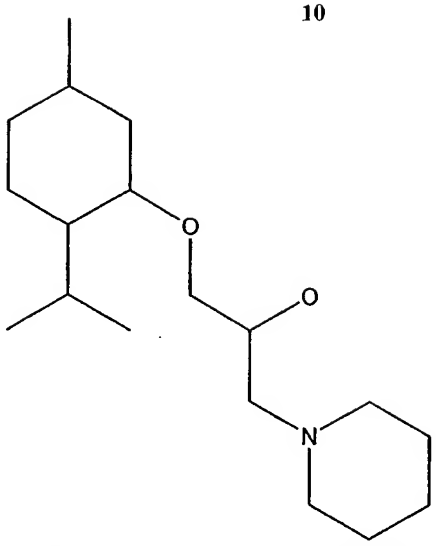


γ,4-Dihydroxy-2-(6-hydroxy-1-heptenyl)-4-cyclopentanecrotonic acidλ-lactone (Brefeldin A)



4-(Benzylidene-amino)-phenol

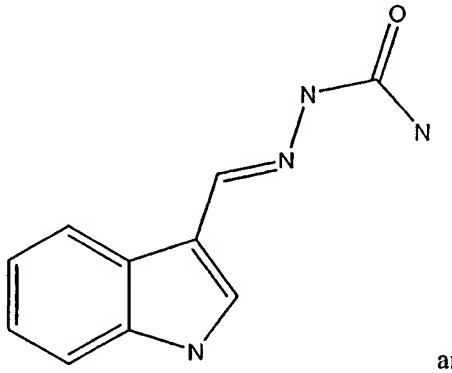




1-(2-Isopropyl-5-methyl-cyclohexyloxy)-3-piperidin-1-yl-propan-2-ol

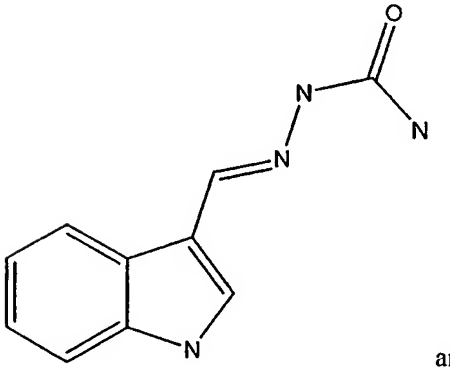
In another aspect of the invention a method for treating a fungal infection in a subject by administering to a subject in need thereof an anti-fungal small molecule. In one embodiment the anti-fungal small molecule is one or more of 8-(N,N-Diethylamino)-octyl-3,4,5-trimethoxybenzoate HCl, Ethyl [2-amino-6-bromo-4-(1-cyano-2-ethoxy-2-oxoethyl)]-4H-chromene-3-carboxylate, N-(3-Chlorophenyl)-6,7-dimethoxy-4-quinazolinamine, [[3,5-bis(1,1-Dimethylethyl)-4-hydroxyphenyl]methylene]propanedinitrile, 8-Chloro-11-(4-methyl-1-piperazinyl)-5H-dibenzo[b,e][1,4]-diazepine, 8-[4,4-bis(p-Fluorophenyl)butyl]-1-phenyl-1,3,8-triazino[4.5]decan-4-one, 2-Chloro-5-nitro-N-phenylbenzamide, 3-(5'-Hydroxymethyl-2'-furyl)-1-benzylindazole, (2S)-2-[[(2S)-2-[(2S,3S)-2-[(2R)-2-Amino-3-mercaptopropyl]amino]-3-methylpentyl]oxy]-1-oxo-3-phenylpropyl]amino]-4-(methylsulfonyl)-butanoic Acid 1-Methylethyl Ester, 3-(3,5-Dibromo-4-hydroxybenzyliden)-5-iodo-1,2-dihydroindol-2-one, 5,8,11,14-eicosatetrayonic acid, *Penicillium palitans* Penitrem A, 1-[β-[3-(4-Methoxyphenyl)propoxy]-4-methoxyphenethyl]-1H-imidazole HCl, N,N,N',N'-*tetrakis*-(2-pyridylmethyl)-ethylenediamine, 3,4-Dihydroxy-a-cyanothiocinnamamide a-Cyano-3,4-dihydroxythiocinnamamide, *Discodermia calyx* Calyculin A, 3-[1-[3-(Amidinothio)propyl-1H-indol-3-yl]-3-(1-methyl-1H-indol-3-yl)maleimide Bisindolylmaleimide IX Methanesulfonate, *Nocardiopsis* K252A, 1-(5-Iodonapthalene-1-sulfonyl)homopiperazine, 1-(5-Chloronapthalene-1-sulfonyl)homopiperazine HCl, *Streptomyces hygroscopicus* Nigericin, γ,4-Dihydroxy-2-(6-hydroxy-1-heptenyl)-4-cyclopentanecrotonic acidλ-lactone, (E)3-[(4-Methylphenyl)sulfonyl]-2-propenenitrile, 3-Hexadecanoyl-5-hydroxymethyl-tetronic Acid,

Tabebuia avellanedae Beta-lapachone, 2,4-Dichlorobenzamil, 2-Thioureido-L-norvaline, 6-Anilino-5,8-quinolinequinone, Diphenyleneiodonium Cl, Manumycin A, Lycorine, 3,5-Diamino-6-chloro-N-[imino(phenylamino)methyl]pyrazinecarboxamide, 1,2-Dihydro-3H-naphtho[2,1-b]pyran-3-one, 1-(6-(17β-3-methoxyestra-1,3,5(10)-trien-17-yl)amino)hexyl)-1H-pyrrole-2,5-dione, 1-(3,6-Dibromocarbazol-9-yl)-3-dimethylaminopropan-2-ol, N_1N-dimethylsphingosine, 1-hexadecyl-2-methylglycero-3-phosphatidylcholine, 1-octadecyl-2-methylglycero-3-phosphatidylcholine, 3,4-dichloroisocoumarin, 5,8,11-eicosatriyonic acid, 4-(Benzylidene-amino)-phenol, 1-(2-isopropyl-5-methyl-cyclohexyloxy)-3-piperidin-1-yl-propan-2-ol, or



and analogs and salts thereof.

In an embodiment of the invention the anti-fungal small molecule is 4-(benzylidene-amino)-phenol and 2-Chloro-5-nitro-N-phenylbenzamide analogs or salts thereof. In another embodiment of the invention the anti-fungal small molecule is



and 8-Chloro-11-(4-methyl-1-piperazinyl)-5H-dibenzo[b,e][1,4]-diazepine analogs or salts thereof. In a further embodiment of the invention the anti-fungal small molecule is 1-(2-isopropyl-5-methyl-cyclohexyloxy)-3-piperidin-1-yl-propan-2-ol and 8-Chloro-11-(4-methyl-1-piperazinyl)-5H-dibenzo[b,e][1,4]-diazepine analogs or salts thereof. In another embodiment of the invention the anti-fungal small molecule is 4-(benzylidene-amino)-phenol and ethyl [2-amino-6-bromo-4-(1-cyano-2-ethoxy-2-oxoethyl)]-4H-chromene-3-carboxylate.

In an embodiment of the invention the fungal infection is one or more of *Candida albicans*, *Pneumocystis carinii*, *Saccharomyces cerevisiae*, *Aspergillus nidulans*, *Kluyveromyces lactis*, *Schizosaccharomyces pombe*, *Streptomyces lasaliensis*, *Streptomyces hygroscopicus*, *Candida tropicalis*, *Candida dubliniensis*, *Candida parapsilosis*, *Candida kefyr*, *Candida guilliermondii*, *Candida inconspicua*, *Candida famata*, *Candida glabrata*, *Candida krusei*, *Candida lusitaniae*, *Cryptococcus neoformans*, *Coccidioides immitis*, or *Hispolasma capsulatum*. In a second embodiment the fungal infection is a pathogenic yeast. In another embodiment the fungal infection is *Candida albicans*.

In one embodiment of the invention the subject is a human. In another embodiment the subject is immunocompromised. In another embodiment the subject has had chemotherapy. In a further embodiment the subject has AIDS. In still further embodiments the subject has a central venous catheter.

In an embodiment of the invention the anti-fungal molecule is administered via injection, topical route, oral route, nasal route, aerosol, or enema route. In one embodiment the anti-fungal small molecule is administered via an oral route. In a second embodiment the anti-fungal small molecule is administered via a topical route.

In an aspect of the invention a composition comprising an anti-fungal small molecule and an anti-fungal agent is provided, which may optionally be a topical lotion. A topical lotion comprising an anti-fungal small molecule and a topical carrier is also provided according to other aspects of the invention. In some embodiments the anti-fungal small molecule is one or more of the anti-fungal small molecules listed above and/or described herein.

In an embodiment of the invention the anti-fungal agent is an anti-*Candida albicans* agent. In a second embodiment the anti-*Candida albicans* agent is one or more of Acrisorcin; Ambruticin; Amphotericin B; Azaconazole; Azaserine; Basifungin; Bifonazole; Biphenamine Hydrochloride ; Bispyrithione Magsulfex ; Butoconazole Nitrate; Calcium Undecylenate; Candicidin; Carbol-Fuchsin; Chlordantoin; Ciclopirox; Ciclopirox Olamine; Cilofungin; Cisconazole; Clotrimazole; Cuprimyxin; Denofungin ; Dipyrithione; Doconazole; Econazole; Econazole Nitrate; Enilconazole; Ethonam Nitrate; Fenticonazole Nitrate; Filipin; Fluconazole; Flucytosine; Fungimycin; Griseofulvin; Hamycin; Isoconazole ; Itraconazole; Kalafungin; Ketoconazole; Lomofungin; Lydimycin; Mepartricin ; Miconazole; Miconazole Nitrate; Monensin ; Monensin Sodium ; Naftifine Hydrochloride; Neomycin Undecylenate ; Nifuratel ; Nifurmerone; Nitralamine Hydrochloride; Nystatin; Octanoic Acid; Orconazole Nitrate; Oxiconazole Nitrate; Oxifungin Hydrochloride; Parconazole Hydrochloride; Partricin

; Potassium Iodide ; Proclonol ; Pyrithione Zinc ; Pyrrolnitrin; Rapamycin; Rutamycin; Sanguinarium Chloride ; Saperconazole; Scopafungin ; Selenium Sulfide ; Sinefungin; Sulconazole Nitrate; Tamoxifen; Terbinafine; Terconazole; Thiram; Ticlatone ; Tioconazole; Tolciclate; Tolindate; Tolnaftate; Triacetin; Triafungin; Tunicamycin; Undecylenic Acid; Viridofulvin; Zinc Undecylenate; or Zinoconazole Hydrochloride.

In one embodiment of the invention the topical lotion is formulated as a cream, an ointment, drops, a gel, a controlled-release patch, a spray, a pessary, or a foam.

In an embodiment of the invention the topical carrier is one or more of mineral oil, sorbitan monostearate, polysorbate 60, cetyl esters wax, cetearyl alcohol, 2-octyldodecanol, benzyl alcohol, liquid petroleum, white petroleum, propylene glycol, polyoxyethylene polyoxypropylene compound, emulsifying wax or water.

Detailed Description of the Invention

Methods for reducing the growth of a fungus using anti-fungal small molecules have been discovered. Applicants have discovered that specific classes of molecules are effective in reducing the growth and for inhibiting the yeast-to-hyphal transition of fungi. These molecules are thus, useful for a variety of *in vitro* and *in vivo* uses, such as those described herein.

In an aspect of the invention a fungal cell is contacted with an anti-fungal small molecule in an amount effective to reduce the fungal cell growth. It is intended that the fungal cell is contacted either *in vitro* or *in situ*, whereby *in situ* includes contacting a fungal cell *in vivo* or contacting a fungal cell on the surface of the skin. One of ordinary skill in the art would understand "contacting" to encompass putting a fungal cell into contact with an anti-fungal small molecule for example in a tissue culture plate whereby the fungal cell is placed into a media environment and an anti-fungal small molecule is added to the media. Further "contacting" would be understood by one of ordinary skill in the art to mean adding an anti-fungal small molecule to a fungal cell or population of fungal cells on the surface of the skin or parenterally or locally applying an anti-fungal agent to a subject such that the fungus in the subject is exposed to the anti-fungal agent.

A fungal cell is intended to encompass any cell originating from a fungal species or fungus. As used herein a fungus is also intended to include moulds, yeast and pathogenic yeast. A fungus includes but is not limited to *Candida* for example *Candida albicans, Candida tropicalis, Candida dubliniensis, Candida parapsilosis, Candida kefyr, Candida guilliermondii, Candida inconspicua, Candida famata, Candida glabrata, Candida krusei,*

and *Candida lusitaniae*, *Pneumocystis* for example *Pneumocystis carinii*, *Saccharomyces* for example *Saccharomyces cerevisiae*, *Aspergillus* for example *Aspergillus nidulans*, *Kluyveromyces* for example *Kluyveromyces lactis*, *Schizosaccharomyces* for example *Schizosaccharomyces pombe*, and *Streptomyces* for example *Streptomyces lasaliensis* and *Streptomyces hygroscopicus*, *Cryptococcus neoformans*, *Coccidioides immitis*, and *Hispolasma capsulatum*. In some embodiments the fungus is a pathogenic yeast, such as *Candida albicans*.

In some instances the compounds described herein are useful also for treating a fungal infection in a subject. As used herein treating or treat is intended to include preventing, ameliorating, curing, reducing fungal growth or reducing symptoms, or preventing any increase in fungal growth or symptoms.

As used herein "reducing fungal growth" is intended to encompass an interference in fungal cell growth or processing which can be determined by a reduction in cell number, a reduction in cell division or a reduction in the yeast-to-hyphal transition phase.

Methods for detecting a reduction in fungal growth are known to those of skill in the art and include high throughput assays. A novel example of such a method is described in U.S. application serial no. 60/445,314 and corresponding PCT application serial no. PCT/US04/03208 designating the US, both of which are incorporated herein by reference. Generally fungal cells are grown in microtitre plates and incubated with a molecule of the invention to determine reduction of fungal cell growth. For example, *C. albicans* cells are grown in YNB media that inhibits hyphal growth and then transferred to 384-well optical plates containing Spider media to induce the budded-to-hyphal transition and hyphal elongation. The yeast-to-hyphal morphological transition is essential for the virulence of *C. albicans*. An anti-fungal small molecule is added, incubated at 37°C for 4 hours and inhibition or reduction of fungal growth determined. One of skill in the art would be able to detect a reduction in growth by routine methods such as microscopy. YNB media is well known in the art and contains yeast nitrogen base (DIFCO Labs.), glucose (US Biological) and d-H_2O. Spider media is well known in the art and contains nutrient broth (DIFCO Labs.), mannitol (Sigma – Aldrich), K_2HPO_4 (Sigma – Aldrich) and d-H_2O.

Other methods for determining a reduction in fungal growth include methods for determining the number of fungal cells using cell staining techniques such as trypan blue and counting the cells using a microscope. Methods such as PCR and RT-PCR are contemplated for determining a reduction of RNA or DNA as a measure of reduced fungal growth. Other methods include observation of a visible reduction of the fungal infection as a result of

reduced fungal growth. These methods are well known to those of ordinary skill in the art and require routine procedures.

A "subject" as used herein is any animal in need of treatment, including humans, primates and other mammals such as equines, cattle, swine, sheep, goats, primates, mice, rats, and pets in general including dogs, cats, guinea pigs, ferrets, and rabbits.

As used herein subject in need thereof is a subject having a fungal infection, or a subject at risk of developing a fungal infection. The subject may have been diagnosed as having such a fungal infection as described herein or using standard medical techniques known to those of skill in the art. Alternatively a subject may exhibit one or more symptoms of fungal infection.

A subject at risk of developing a fungal infection is a subject who has been exposed to a fungus, or is susceptible to exposure to a fungus. For instance a subject that is susceptible to exposure to a fungus includes those subjects who work with fungal material or in areas of high fungal content, subjects who travel to areas with high fungal infectivity rates or are otherwise likely to be exposed to a fungal infection as well as those subjects having particular susceptibility to fungal infection resulting from medical conditions or therapies. Examples of subjects having particular susceptibility to fungal infections arising from medical conditions or therapies include but are not limited to an immunocompromised subject, a subject having received chemotherapy, a subject having cancer, a subject having AIDS, a subject who is HIV positive, a subject who is at risk of being HIV positive, a subject having received a transplant, or a subject having a central venous catheter.

An immunocompromised subject is a subject that is incapable of inducing a normal effective immune response or a subject that has not yet developed an immune system (e.g. preterm neonate). An immunocompromised subject, for example, is a subject undergoing or undergone chemotherapy, a subject having AIDS, a subject receiving or having received a transplant or other surgical procedure etc.

A subject having received chemotherapy is a subject that has undergone some form of chemotherapeutic procedure. Chemotherapeutic procedure encompasses conventional methods known to those of skill in the art. Examples of chemotherapeutic methods include but are not limited to alkylating agents, for example, nitrogen mustards, ethyleneimine compounds and alkyl sulphonates; antimetabolites, for example, folic acid, purine or pyrimidine antagonists, mitotic inhibitors, for example, vinca alkaloids and derivatives of podophyllotoxin; cytotoxic antibiotics; compounds that damage or interfere with DNA

expression; and growth factor receptor antagonists; antibodies and other biological molecules known to those of ordinary skill in the art.

A subject having cancer is a subject that has detectable cancerous cells. The cancer may be a malignant or non-malignant cancer. Cancers or tumors include but are not limited to biliary tract cancer; brain cancer including glioblastomas and medulloblastomas; bladder cancer; breast cancer; cervical cancer; choriocarcinoma; colon cancer including colorectal carcinomas; endometrial cancer; esophageal cancer; gastric cancer; head and neck cancer; hematological neoplasms including acute lymphocytic and myelogenous leukemia; AIDS-associated leukemias and adult T-cell leukemia lymphoma; intraepithelial neoplasms including Bowen's disease and Paget's disease; lymphomas including Hodgkin's disease and lymphocytic lymphomas; liver cancer; lung cancer (e.g. small cell and non-small cell); melanoma; neuroblastomas; multiple myeloma; oral cancer including squamous cell carcinoma; osteosarcomas; ovarian cancer including those arising from epithelial cells, stromal cells, germ cells and mesenchymal cells; pancreas cancer; prostate cancer; rectal cancer; sarcomas including leiomyosarcoma, rhabdomyosarcoma, liposarcoma, fibrosarcoma, synovial sarcoma and osteosarcoma; skin cancer including melanomas, Kaposi's sarcoma, basocellular cancer, and squamous cell cancer; testicular cancer including germinal tumors such as seminoma, non-seminoma (teratomas, choriocarcinomas), stromal tumors, and germ cell tumors; thyroid cancer including thyroid adenocarcinoma and medullar carcinoma; transitional cancer and renal cancer including adenocarcinoma and Wilms tumor, as well as other carcinomas and sarcomas.

A subject who is HIV positive encompasses a subject who is a carrier of any of the HIV family of retroviruses or a subject who is diagnosed of active AIDS, as well as a subject having AIDS-related conditions. A carrier of HIV may be identified by any methods known in the art. For example, a subject can be identified as an HIV carrier on the basis that the subject is anti-HIV antibody positive, or is HIV-positive, or has symptoms of AIDS. HIV infection generally encompasses infection of a host, particularly a human host, by the human immunodeficiency virus (HIV) family of retroviruses including, but not limited to, HIV I, HIV II, HIV III (also known as HTLV-II, LAV-1, LAV-2), and the like. "HIV" can be used herein to refer to any strains, forms, subtypes and variations in the HIV family. A subject having HIV is a subject who is at any one of the several stages of HIV infection progression, which, for example, include acute primary infection syndrome (which can be asymptomatic or associated with an influenza-like illness with fevers, malaise, diarrhea and neurologic symptoms such as headache), asymptomatic infection (which is the long latent period with a

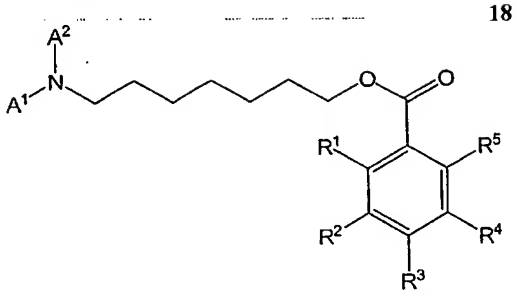
gradual decline in the number of circulating CD4+ T cells), and AIDS (which is defined by more serious AIDS-defining illnesses and/or a decline in the circulating CD4 cell count to below a level that is compatible with effective immune function). In addition, it is intended to encompass subjects suspected of being infected with HIV after suspected past exposure to HIV by e.g., contact with HIV-contaminated blood, blood transfusion, exchange of body fluids, "unsafe" sex with an infected subject, accidental needle stick, receiving a tattoo or acupuncture with contaminated instruments, or transmission of the virus from a mother to a baby during pregnancy, delivery or shortly thereafter. Subjects who are HIV positive also encompass subjects who have not been diagnosed as having HIV infection but are believed to be at high risk of infection by HIV.

A subject having acquired immunodeficiency syndrome (AIDS) is a subject who exhibits more serious AIDS-defining illnesses and/or a decline in the circulating CD4 cell count to below a level that is compatible with effective immune function. A subject having AIDS also encompasses a subject having AIDS-related conditions, which means disorders and diseases incidental to or associated with AIDS or HIV infection such as AIDS-related complex (ARC), progressive generalized lymphadenopathy (PGL), anti-HIV antibody positive conditions, and HIV-positive conditions, AIDS-related neurological conditions (such as dementia or tropical paraparesis), Kaposi's sarcoma, thrombocytopenia purpurea and associated opportunistic infections such as Pneumocystis carinii pneumonia, Mycobacterial tuberculosis, esophageal candidiasis, toxoplasmosis of the brain, CMV retinitis, HIV-related encephalopathy, HIV-related wasting syndrome, etc.

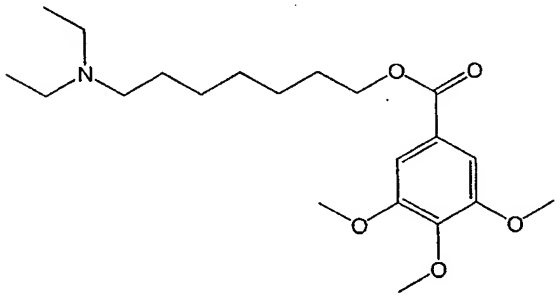
A subject having received a transplant is a subject having received either a tissue or organ transplant during a surgical procedure. Transplants include but are not limited to organ, tissue, stem cell, bone marrow, and encompass conventional methods known to those of skill in the art. A subject having received a tissue transplant is especially susceptible to fungal infections from *Candida* species such as *Candida albicans*.

A subject having a central venous catheter is a subject having received a central venous catheter implant during a surgical procedure. A central venous catheter implant encompasses the use of conventional methods known to those of skill in the art. A subject having received a central venous catheter is especially susceptible to fungal infections from *Candida* species such as *Candida albicans*.

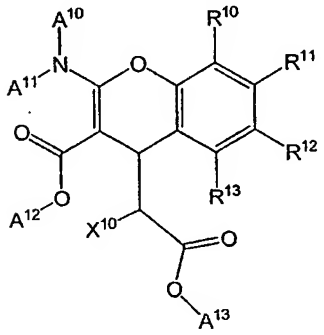
In an aspect of the invention an anti-fungal small molecule, analog or salt thereof has the following structure:



In an embodiment each of A^1 and A^2 independently is one of –H or an alkyl; and each of R^1, R^2, R^3, R^4, and R^5 independently is one of –H, a halogen, an alkyl, –OH, or an alkoxy. In a second embodiment each of A^1 and A^2 independently is an alkyl. In another embodiment each of A^1 and A^2 is ethyl. In one embodiment at least one of R^1, R^2, R^3, R^4, or R^5 is an alkoxy. In a second embodiment at least two of R^1, R^2, R^3, R^4, or R^5 independently is an alkoxy. In another embodiment at least three of R^1, R^2, R^3, R^4, or R^5 independently is an alkoxy. In a further embodiment at least one of R^1, R^2, R^3, R^4, or R^5 is methoxy. In yet another embodiment each of R^2, R^3, and R^4 is methoxy. In further embodiments each of R^1 and R^5 is –H. In a preferred embodiment the anti-fungal small molecule has the following structure:

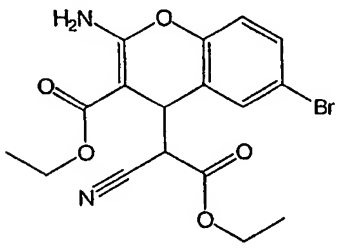


In an aspect of the invention an anti-fungal small molecule, analog or salt thereof has the following structure:

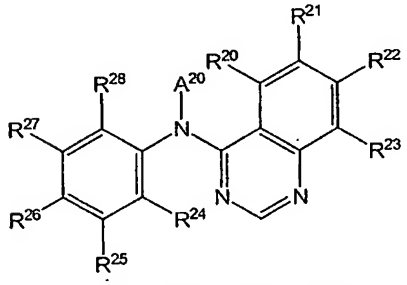


In an embodiment each of A^{10}, A^{11}, A^{12}, and A^{13} independently is one of –H or an alkyl; X^{10} is –CN or a halogen; and each of R^{10}, R^{11}, R^{12}, and R^{13} independently is one of –H, a halogen, an alkyl, –OH, or an alkoxy. In a second embodiment at least one of R^{10}, R^{11}, R^{12},

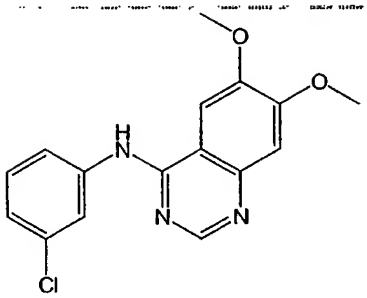
or R^{13} is a halogen. In another embodiment at least one of R^{10}, R^{11}, R^{12}, or R^{13} is –Br. In a further embodiment R^{12} is –Br. In yet another embodiment each of R^{10}, R^{11}, and R^{13} is –H. In still another embodiment X^{10} is –CN. In an embodiment each of A^{10} and A^{11} is –H. In a second embodiment A^{12} is an alkyl. In another embodiment A^{12} is ethyl. In a further embodiment A^{13} is an alkyl. In yet another embodiment A^{13} is ethyl. In a preferred embodiment the anti-fungal small molecule has the following structure:



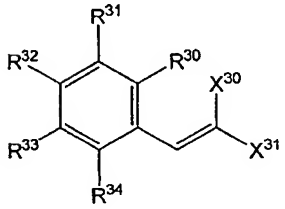
In an aspect of the invention an anti-fungal small molecule, analog or salt thereof has the following structure:



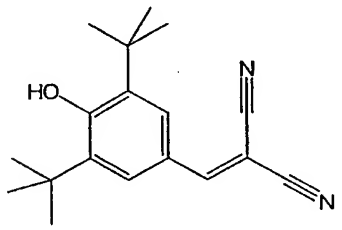
In an embodiment A^{20} is one of –H or an alkyl; and each of R^{20}, R^{21}, R^{22}, R^{23}, R^{24}, R^{25}, R^{26}, R^{27}, and R^{28} independently is one of –H, a halogen, an alkyl, –OH, or an alkoxy. In a second embodiment A^{20} is –H. In another embodiment at least one of R^{20}, R^{21}, R^{22}, or R^{23} is an alkoxy. In a further embodiment at least two of R^{20}, R^{21}, R^{22}, or R^{23} independently is an alkoxy. In yet another embodiment at least one of R^{20}, R^{21}, R^{22}, or R^{23} is methoxy. In still another embodiment each of R^{21} and R^{22} is methoxy. In another embodiment each of R^{20} and R^{23} is –H. In an embodiment at least one of R^{24}, R^{25}, R^{26}, R^{27}, or R^{28} is a halogen. In a second embodiment at least one of R^{24}, R^{25}, R^{26}, R^{27}, or R^{28} is –Cl. In another embodiment R^{25} is –Cl. In a further embodiment each of R^{24}, R^{26}, R^{27}, and R^{28} is –H. In a preferred embodiment the anti-fungal small molecule has the following structure:



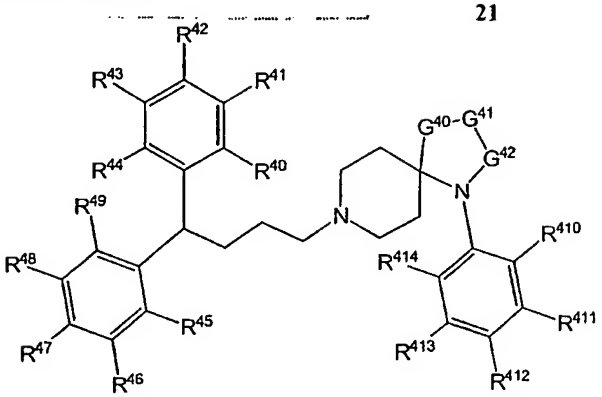
In an aspect of the invention an anti-fungal small molecule, analog or salt thereof has the following structure:



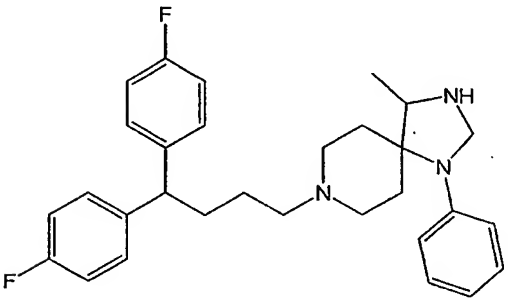
In an embodiment each of X^{30} and X^{31} independently is –CN or a halogen; and each of R^{30}, R^{31}, R^{32}, R^{33}, and R^{34} independently is one of –H, a halogen, an alkyl, –OH, or an alkoxy. In a second embodiment at least one of X^{30} or X^{31} is –CN. In an embodiment each of X^{30} and X^{31} is –CN. In an embodiment at least one of R^{30}, R^{31}, R^{32}, R^{33}, or R^{34} is –OH. In a second embodiment R^{32} is –OH. In another embodiment at least one of R^{30}, R^{31}, R^{32}, R^{33}, or R^{34} is an alkyl. In a further embodiment at least two of R^{30}, R^{31}, R^{32}, R^{33}, or R^{34} independently is an alkyl. In yet another embodiment at least one of R^{30}, R^{31}, R^{32}, R^{33}, or R^{34} is *t*-butyl. In still another embodiment each of R^{31} and R^{33} is *t*-butyl. In another embodiment each of R^{30} and R^{34} is –H. In a preferred embodiment the anti-fungal small molecule has the following structure:



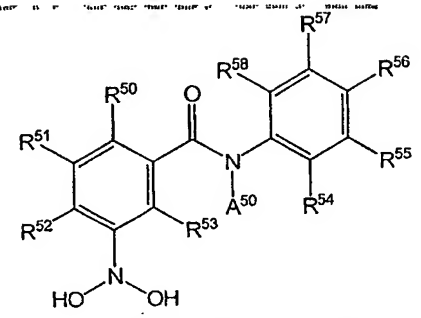
In an aspect of the invention an anti-fungal small molecule, analog or salt thereof has the following structure:



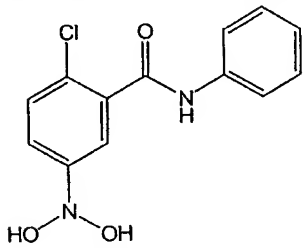
In an embodiment each of R^{40}, R^{41}, R^{42}, R^{43}, R^{44}, R^{45}, R^{46}, R^{47}, R^{48}, R^{49}, R^{410}, R^{411}, R^{412}, R^{413}, and R^{414} independently is one of –H, a halogen, an alkyl, –OH, or an alkoxy; and each of G^{40}, G^{41}, and G^{42} independently is one of or , R at each occurrence independently being one of –H or an alkyl. In a second embodiment at least one of R^{40}, R^{41}, R^{42}, R^{43}, or R^{44} is a halogen. In another embodiment at least one of R^{40}, R^{41}, R^{42}, R^{43}, or R^{44} is –F. In a further embodiment R^{42} is –F. In yet another embodiment each of R^{40}, R^{41}, R^{43}, and R^{44} is –H. In still another embodiment at least one of R^{45}, R^{46}, R^{47}, R^{48}, or R^{49} is a halogen. In a further embodiment at least one of R^{45}, R^{46}, R^{47}, R^{48}, or R^{49} is –F. In another embodiment R^{47} is –F. In yet another embodiment each of R^{45}, R^{46}, R^{48}, and R^{49} is –H. In still another embodiment each of R^{410}, R^{411}, R^{412}, R^{413}, and R^{414} is –H. In an embodiment at least one of G^{40}, G^{41}, or G^{42} is  . In a second embodiment G^{41} is  . In another embodiment G^{41} is  . In a further embodiment G^{40} is  . In yet another embodiment G^{42} is  . In a preferred embodiment the anti-fungal small molecule has the following structure:



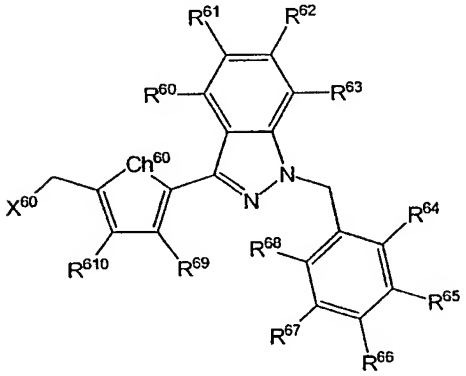
In an aspect of the invention an anti-fungal small molecule, analog or salt thereof has the following structure:



In an embodiment A^{50} is one of –H or an alkyl; and each of R^{50}, R^{51}, R^{52}, R^{53}, R^{54}, R^{55}, R^{56}, R^{57}, and R^{58} independently is one of is one of –H, a halogen, an alkyl, –OH, or an alkoxy. In a second embodiment at least one of R^{50}, R^{51}, R^{52}, or R^{53} is a halogen. In another embodiment at least one of R^{50}, R^{51}, R^{52}, or R^{53} is –Cl. In a further embodiment R^{50} is –Cl. In yet another embodiment each of R^{51}, R^{52}, and R^{53} is –H. In still a further embodiment each of R^{54}, R^{55}, R^{56}, R^{57}, and R^{58} is –H. In another embodiment A^{50} is –H. In a preferred embodiment the anti-fungal small molecule has the following structure:

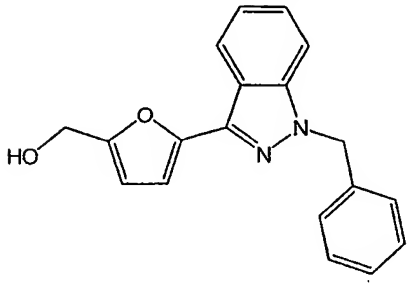


In an aspect of the invention an anti-fungal small molecule, analog or salt thereof has the following structure:

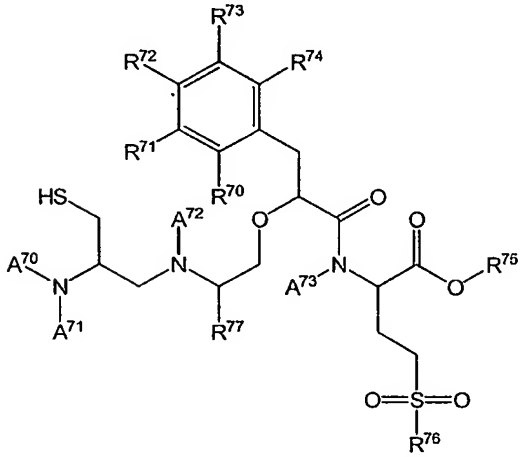


In an embodiment Ch^{60} is a chalcogen; X^{60} is one of –H, –OH, or a halogen; and each of R^{60}, R^{61}, R^{62}, R^{63}, R^{64}, R^{65}, R^{66}, R^{67}, R^{68}, R^{69}, and R^{610} independently is one of –H, a halogen, an alkyl, –OH, or an alkoxy. In a second embodiment Ch^{60} is oxygen. In another embodiment X^{60} is –OH. In a further embodiment each of R^{60}, R^{61}, R^{62}, and R^{63} is –H. In yet another embodiment each of R^{64}, R^{65}, R^{66}, R^{67}, and R^{68} is –H. In still further

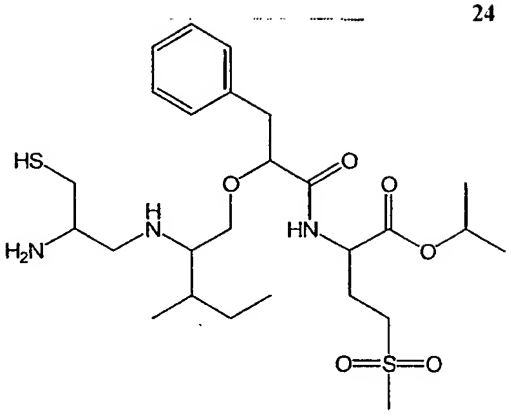
embodiments each of R[510] and R[510] is –H. In a preferred embodiment the anti-fungal small molecule has the following structure:



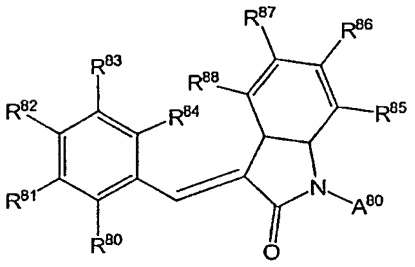
In an aspect of the invention an anti-fungal small molecule, analog or salt thereof has the following structure:



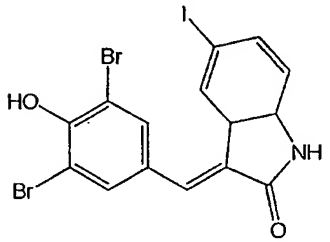
In an embodiment each of A^{70}, A^{71}, A^{72}, and A^{73} independently is one of –H or an alkyl; and each of R^{70}, R^{71}, R^{72}, R^{73}, R^{74}, R^{75}, R^{76}, and R^{77} independently is one of –H, a halogen, an alkyl, –OH, or an alkoxy. In a second embodiment each of A^{70} and A^{71} is –H. In another embodiment A^{72} is –H. In a further embodiment A^{73} is –H. In yet another embodiment each of R^{70}, R^{71}, R^{72}, R^{73}, and R^{74} is –H. In still another embodiment R^{75} is an alkyl. In another embodiment R^{75} is isopropyl. In a further embodiment R^{76} is an alkyl. In yet another embodiment R^{76} is methyl. In still another embodiment R^{77} is an alkyl. In still further embodiments R^{77} is *sec*-butyl. In a preferred embodiment the anti-fungal small molecule has the following structure:



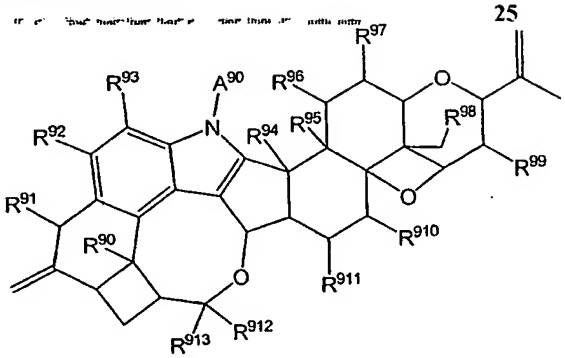
In an aspect of the invention an anti-fungal small molecule, analog or salt thereof has the following structure:



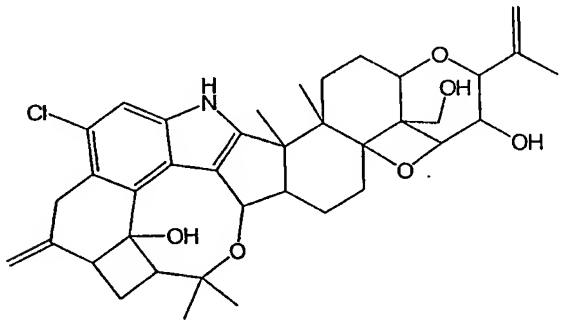
In an embodiment A^{80} independently is one of –H or an alkyl; and each of R^{80}, R^{81}, R^{82}, R^{83}, R^{84}, R^{85}, R^{86}, R^{87}, and R^{88} independently is one of –H, a halogen, an alkyl, –OH, or an alkoxy. In a second embodiment A^{80} is –H. In another embodiment at least one of R^{80}, R^{81}, R^{82}, R^{83}, or R^{84} is a halogen. In a further embodiment at least two of R^{80}, R^{81}, R^{82}, R^{83}, or R^{84} independently is a halogen. In yet another embodiment at least one of R^{80}, R^{81}, R^{82}, R^{83}, or R^{84} is –Br. In another embodiment each of R^{31} and R^{33} is –Br. In still another embodiment at least one of R^{80}, R^{81}, R^{82}, R^{83}, or R^{84} is –OH. In further embodiments R^{82} is –OH. In another embodiment each of R^{80} and R^{84} is –H. In a further embodiment at least one of R^{85}, R^{86}, R^{87}, or R^{88} is a halogen. In still further embodiments at least one of R^{85}, R^{86}, R^{87}, or R^{88} is –I. In a further embodiment each of R^{85}, R^{86}, and R^{88} is –H. In a preferred embodiment the anti-fungal small molecule has the following structure:



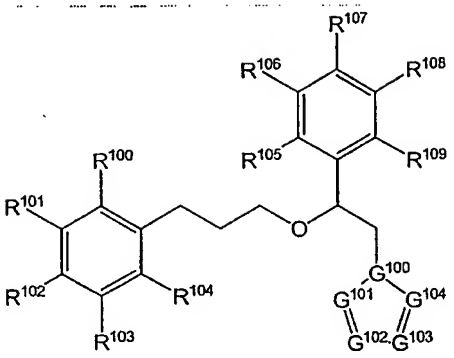
In an aspect of the invention an anti-fungal small molecule, analog or salt thereof has the following structure:



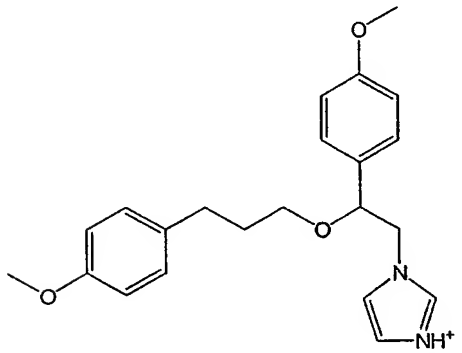
In an embodiment A^{90} independently is one of –H or an alkyl; and each of R^{91}, R^{92}, R^{93}, R^{94}, R^{95}, R^{96}, R^{97}, R^{98}, R^{99}, R^{910}, R^{911}, R^{912}, and R^{913} independently is one of –H, a halogen, an alkyl, –OH, or an alkoxy. In a second embodiment A^{90} is –H. In another embodiment R^{90} is –OH. In a further embodiment at least one of R^{92} or R^{93} is a halogen. In yet another embodiment at least one of R^{92} or R^{93} is –Cl. In still further embodiments R^{92} is –Cl. In another embodiment R^{93} is –H. In an embodiment at least one of R^{94} or R^{95} is an alkyl. In another embodiment each of R^{94} and R^{95} independently is an alkyl. In a further embodiment each of R^{94} and R^{95} is methyl. In yet another embodiment R^{98} is –OH. In still another embodiment R^{99} is –OH. In an embodiment at least one of R^{912} or R^{913} is an alkyl. In another embodiment each of R^{912} and R^{913} independently is an alkyl. In a further embodiment each of R^{912} and R^{913} is methyl. In yet another embodiment R^{91} is –H. In still another embodiment each of R^{96} and R^{97} is –H. In a further embodiment each of R^{910} and R^{911} is –H. In a preferred embodiment the anti-fungal small molecule has the following structure:



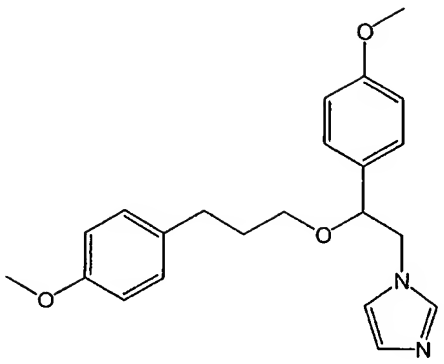
In an aspect of the invention an anti-fungal small molecule, analog or salt thereof has the following structure:



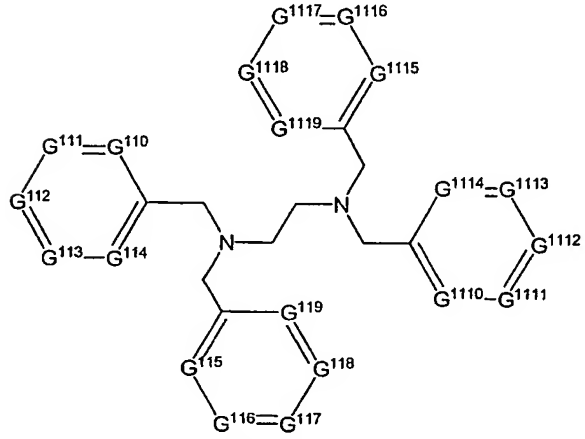
In one embodiment each of R^{100}, R^{102}, R^{103}, R^{104}, R^{105}, R^{106}, R^{107}, R^{108}, and R^{109} independently is one of –H, a halogen, an alkyl, –OH, or an alkoxy; and each of G^{100}, G^{101}, G^{102}, G^{103}, and G^{104} independently is one of N, NH^+ or CR, R at each occurrence independently being one of –H or an alkyl. In a second embodiment only one of G^{100}, G^{101}, G^{102}, G^{103}, and G^{104} is NH^+. In another embodiment G^{103} is NH^+. In a further embodiment G^{100} is N. In yet another embodiment each of G^{101}, G^{102}, and G^{104} is CH. In still another embodiment at least one of R^{100}, R^{102}, R^{103}, or R^{104} is an alkoxy. In yet a further embodiment at least one of R^{100}, R^{102}, R^{103}, or R^{104} is methoxy. In still a further embodiment R^{102} is methoxy. In another embodiment at least one of R^{105}, R^{106}, R^{107}, R^{108}, or R^{109} is an alkoxy. In still another embodiment at least one of R^{105}, R^{106}, R^{107}, R^{108}, or R^{109} is methoxy. In a further embodiment R^{107} is methoxy. In another embodiment the anti-fungal small molecule has the following structure:



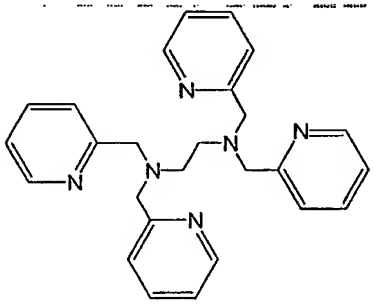
In a preferred embodiment the anti-fungal small molecule has the following structure:



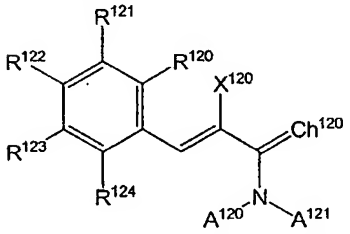
In an aspect of the invention an anti-fungal small molecule, analog or salt thereof has the following structure:



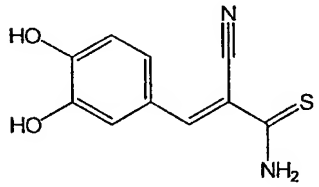
In an embodiment each of G^{110}, G^{111}, G^{112}, G^{113}, G^{114}, G^{115}, G^{116}, G^{117}, G^{118}, G^{119}, G^{1110}, G^{1111}, G^{1112}, G^{1113}, G^{1114}, G^{1115}, G^{1116}, G^{1117}, G^{1118}, and G^{1119} independently is one of N or CR, R at each occurrence independently being one of –H or an alkyl. In a second embodiment at least one of G^{110}, G^{111}, G^{112}, G^{113}, or G^{114} is N. In another embodiment at least one of G^{115}, G^{116}, G^{117}, G^{118}, or G^{119} is N. In a further embodiment at least one of G^{1110}, G^{1111}, G^{1112}, G^{1113}, or G^{1114} is N. In yet another embodiment at least one of G^{1115}, G^{1116}, G^{1117}, G^{1118}, or G^{1119} is N. In still another embodiment G^{114} is N. In another embodiment G^{119} is N. In a further embodiment G^{1114} is N. In yet another embodiment G^{1119} is N. In an embodiment each of G^{110}, G^{111}, G^{112}, G^{113}, G^{115}, G^{116}, G^{117}, G^{118}, G^{1110}, G^{1111}, G^{1112}, G^{1113}, G^{1115}, G^{1116}, G^{1117}, and G^{1118} is CH. In a preferred embodiment the anti-fungal small molecule has the following structure:



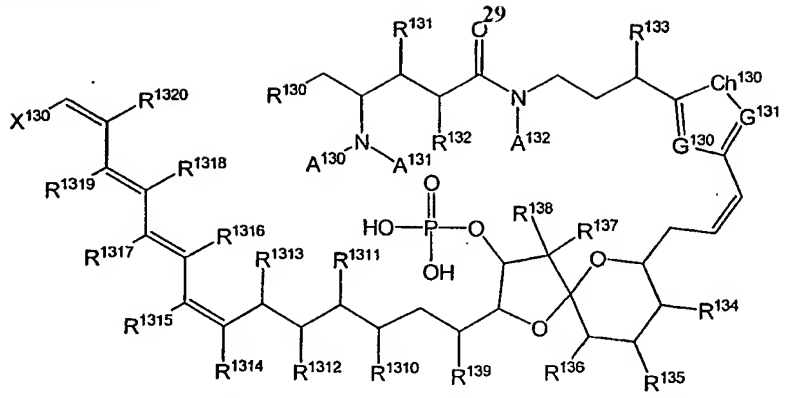
In an aspect of the invention an anti-fungal small molecule, analog or salt thereof has the following structure:



In an embodiment Ch^{120} is a chalcogen; each of A^{120} and A^{121} independently is one of –H or an alkyl; X^{120} is –CN or a halogen; and each of R^{120}, R^{121}, R^{122}, R^{123}, and R^{124} independently is one of –H, a halogen, an alkyl, –OH, or an alkoxy. In a second embodiment Ch^{120} is sulfur. In another embodiment X^{120} is –CN. In a further embodiment at least one of R^{120}, R^{121}, R^{122}, R^{123}, or R^{124} is –OH. In yet another embodiment at least two of R^{120}, R^{121}, R^{122}, R^{123}, or R^{124} independently is –OH. In still further embodiments each of R^{122} and R^{123} is –OH. In another embodiment each of R^{120}, R^{121}, and R^{124} is –OH. In a further embodiment at least one of A^{120} or A^{121} is –H. In yet another embodiment each of A^{120} and A^{121} is –H. In a preferred embodiment the anti-fungal small molecule has the following structure:



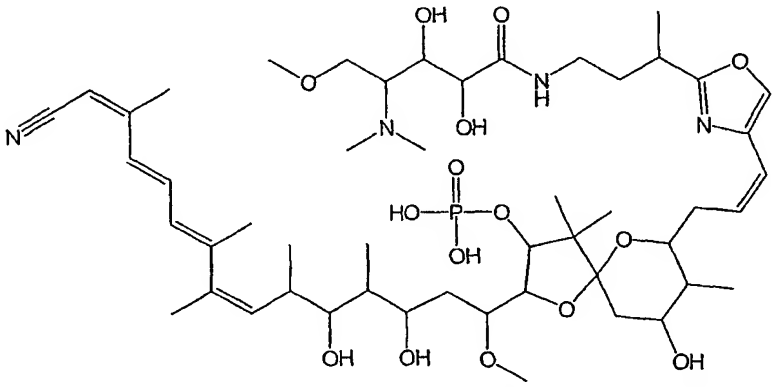
In an aspect of the invention an anti-fungal small molecule, analog or salt thereof has the following structure:



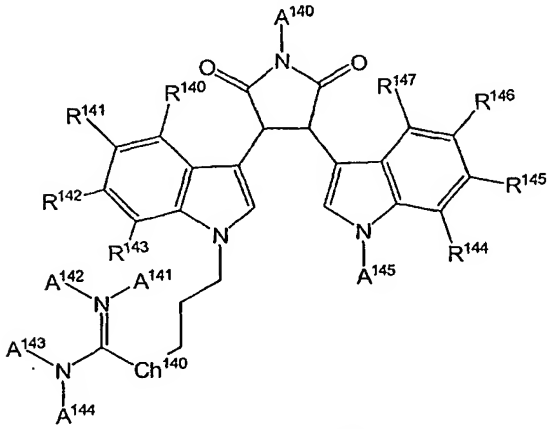
In an embodiment Ch^{130} is a chalcogen; each of A^{130}, A^{131} and A^{132} independently is one of –H or an alkyl; X^{130} is –CN or a halogen; each of R^{130}, R^{131}, R^{132}, R^{133}, R^{134}, R^{135}, R^{136}, R^{137}, R^{138}, R^{139}, R^{1310}, R^{1311}, R^{1312}, R^{1313}, R^{1314}, R^{1315}, R^{1316}, R^{1317}, R^{1318}, R^{1319}, and R^{1320} independently is one of –H, a halogen, an alkyl, –OH, or an alkoxy; and each of G^{130} and G^{131} independently is one of N or CR, R being one of –H or an alkyl. In a second embodiment X^{130} is –CN. In another embodiment Ch^{130} is oxygen. In a further embodiment at least one of G^{130} or G^{131} is N. In yet another embodiment G^{130} is N. In another embodiment G^{131} is CH. In an embodiment at least one of A^{130} or A^{131} is an alkyl. In a second embodiment each of A^{130} and A^{131} independently is an alkyl. In another embodiment each of A^{130} and A^{131} is methyl. In a further embodiment A^{132} is –H. In an embodiment R^{130} is an alkoxy. In another embodiment R^{130} is methoxy. In a further embodiment at least one of R^{131} or R^{132} is –OH. In yet another embodiment each of R^{131} and R^{132} is –OH. In still another embodiment R^{133} is an alkyl. In a further embodiment R^{133} is methyl. In another embodiment at least one of R^{134}, R^{135}, or R^{136} is an alkyl. In a further embodiment R^{134} is an alkyl. In yet another embodiment R^{134} is methyl. In still another embodiment at least one of R^{134}, R^{135}, or R^{136} is –OH. In an embodiment R^{135} is –OH. In another embodiment R^{136} is –H. In a further embodiment at least one R^{137} or R^{138} is an alkyl. In another embodiment each of R^{137} and R^{138} independently is an alkyl. In an embodiment each of R^{137} and R^{138} is methyl. In another embodiment R^{139} is an alkoxy. In a further embodiment R^{139} is methoxy.

In an embodiment at least one of R^{1310}, R^{1311}, R^{1312}, R^{1313}, or R^{1314} is –OH. In a second embodiment at least two of R^{1310}, R^{1311}, R^{1312}, R^{1313}, or R^{1314} independently s –OH. In another embodiment each of R^{1310} and R^{1312} is –OH. In a further embodiment at least one of R^{1310}, R^{1311}, R^{1312}, R^{1313}, or R^{1314} is an alkyl. In yet another embodiment at least two of R^{1310}, R^{1311}, R^{1312}, R^{1313}, or R^{1314} independently is an alkyl. In still another embodiment at least one of R^{1310}, R^{1311}, R^{1312}, R^{1313}, or R^{1314} is methyl. In another embodiment each of R^{1311} and R^{1313} is methyl. In yet another embodiment R^{1314} is –H. In an embodiment at least one of R^{1315},

R^{1316}, R^{1317}, R^{1318}, R^{1319}, or R^{1320} is an alkyl. In a second embodiment at least two of R^{1315}, R^{1316}, R^{1317}, R^{1318}, R^{1319}, or R^{1320} independently is an alkyl. In another embodiment at least three of R^{1315}, R^{1316}, R^{1317}, R^{1318}, R^{1319}, or R^{1320} independently is an alkyl. In a further embodiment at least one of R^{1315}, R^{1316}, R^{1317}, R^{1318}, R^{1319}, or R^{1320} is methyl. In yet another embodiment each of R^{1315}, R^{1316}, and R^{1320} is methyl. In still another embodiment each of R^{1317}, R^{1318}, and R^{1319} is –H. In a preferred embodiment the anti-fungal small molecule has the following structure:

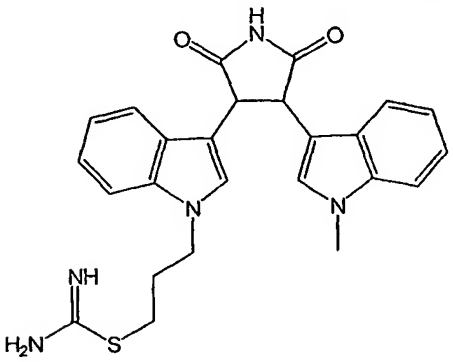


In an aspect of the invention an anti-fungal small molecule, analog or salt thereof has the following structure:

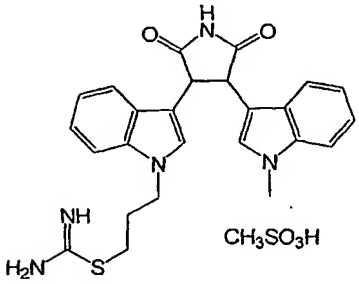


In an embodiment Ch^{140} is a chalcogen; each of A^{140}, A^{141}, A^{142}, A^{143}, A^{144}, and A^{145} independently is one of –H or an alkyl; and each of R^{140}, R^{141}, R^{142}, R^{143}, R^{144}, R^{145}, R^{146}, and R^{147} independently is one of –H, a halogen, an alkyl, –OH, or an alkoxy. In a second embodiment Ch^{140} is sulfur. In another embodiment A^{140} is –H. In a further embodiment at least one of A^{141}, A^{142}, A^{143}, or A^{144} is –H. In yet another embodiment at least two of A^{141}, A^{142}, A^{143}, or A^{144} independently is –H. In still another embodiment each of A^{141}, A^{142}, A^{143}, or A^{144} is –H. In a further embodiment A^{145} is an alkyl. In another embodiment A^{145} is methyl. In still further embodiments each of R^{140}, R^{141}, R^{142}, and R^{143} is –H. In yet another

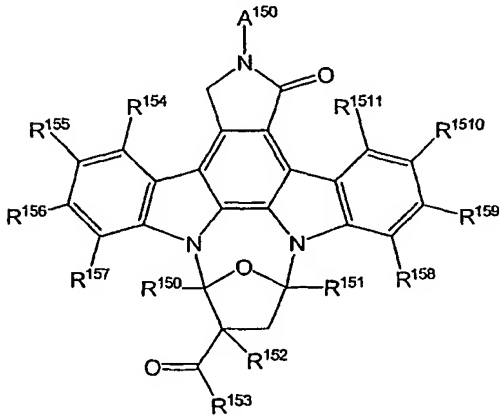
embodiment each of R^{144}, R^{145}, R^{146}, and R^{147} is –H. In a further embodiment the anti-fungal small molecule has the following structure:



In a preferred embodiment the anti-fungal small molecule has the following structure:

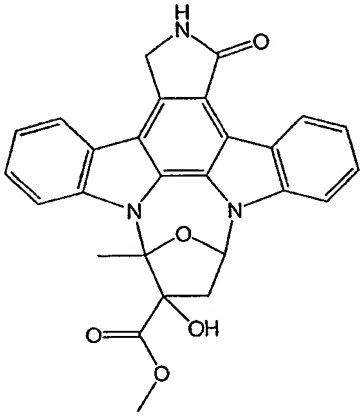


In an aspect of the invention an anti-fungal small molecule, analog or salt thereof has the following structure:

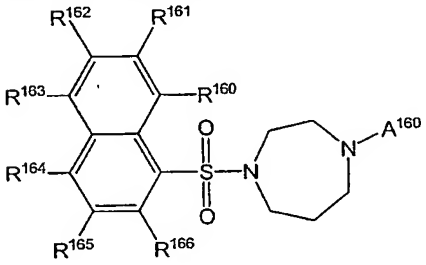


In an embodiment A^{150} is one of –H or an alkyl; and each of R^{150}, R^{151}, R^{152}, R^{153}, R^{154}, R^{155}, R^{156}, R^{157}, R^{158}, R^{159}, R^{1510}, and R^{1511} independently is one of –H, a halogen, an alkyl, –OH, or an alkoxy. In a second embodiment A^{150} is –H. In another embodiment at least one of R^{150} or R^{151} is an alkyl. In a further embodiment R^{150} is an alkyl. In yet another embodiment R^{150} is methyl. In an embodiment R^{151} is –H. In another embodiment R^{152} is –OH. In a further embodiment R^{153} is an alkoxy. In yet another embodiment R^{153} is methoxy.

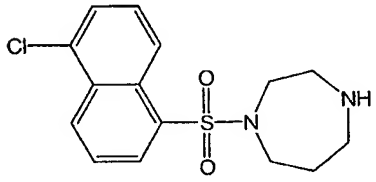
In still further embodiments each of R^{154}, R^{155}, R^{156}, and R^{157} is –H. In another embodiment each of R^{158}, R^{159}, R^{1510}, and R^{1511} is –H. In a preferred embodiment the anti-fungal small molecule has the following structure:



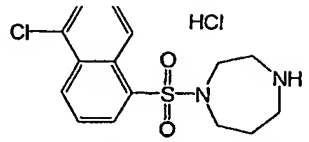
In an aspect of the invention an anti-fungal small molecule, analog or salt thereof has the following structure:



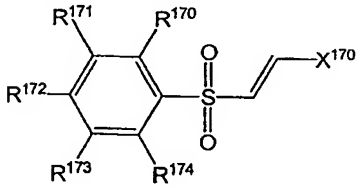
In an embodiment A^{160} is one of –H or an alkyl; and each of R^{160}, R^{161}, R^{162}, R^{163}, R^{164}, R^{165}, and R^{166} independently is one of –H, a halogen, an alkyl, –OH, or an alkoxy. In a second embodiment A^{160} is –H. In another embodiment at least one of R^{160}, R^{161}, R^{162}, R^{163}, R^{164}, R^{165}, or R^{166} is a halogen. In a further embodiment at least one of R^{160}, R^{161}, R^{162}, R^{163}, R^{164}, R^{165}, or R^{166} is –Cl. In yet another embodiment R^{163} is –Cl. In still another embodiment each of R^{160}, R^{161}, R^{162}, R^{164}, R^{165}, and R^{166} is –H. In a preferred embodiment the anti-fungal small molecule has the following structure:



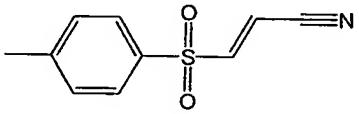
In another preferred embodiment the anti-fungal small molecule has the following structure:



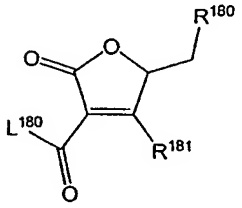
In an aspect of the invention an anti-fungal small molecule, analog or salt thereof has the following structure:



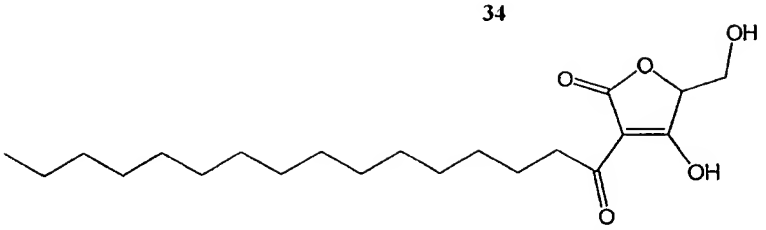
In an embodiment X^{170} is –CN or a halogen; and each of R^{170}, R^{171}, R^{172}, R^{173}, and R^{174} independently is one of –H, a halogen, an alkyl, –OH, or an alkoxy. In a second embodiment X^{170} is –CN. In another embodiment at least one of R^{170}, R^{171}, R^{172}, R^{173}, or R^{174} is an alkyl. In a further embodiment at least one of R^{170}, R^{171}, R^{172}, R^{173}, or R^{174} is methyl. In yet another embodiment R^{172} is methyl. In a further embodiment each of R^{170}, R^{171}, R^{173}, and R^{174} is –H. In a preferred embodiment the anti-fungal small molecule has the following structure:



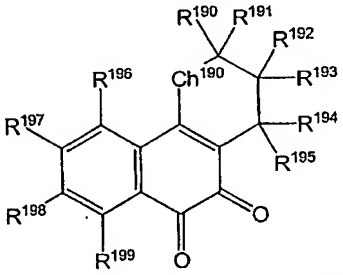
In an aspect of the invention an anti-fungal small molecule, analog or salt thereof has the following structure:



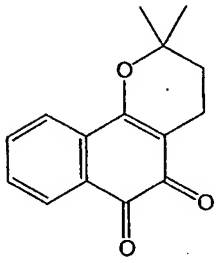
In an embodiment L^{180} is an alkyl comprising at least 10 carbon atoms; and each of R^{180} and R^{181} independently is one of –H, a halogen, an alkyl, –OH, or an alkoxy. In a second embodiment R^{180} is –OH. In another embodiment R^{181} is –OH. In a further embodiment L^{180} comprises at least 12 carbon atoms. In yet another embodiment L^{180} comprises at least 15 carbon atoms. In an embodiment L^{180} is a straight-chain alkyl. In another embodiment L^{180} is a saturated alkyl. In a further embodiment L^{180} is pentadecyl. In a preferred embodiment the anti-fungal small molecule has the following structure:



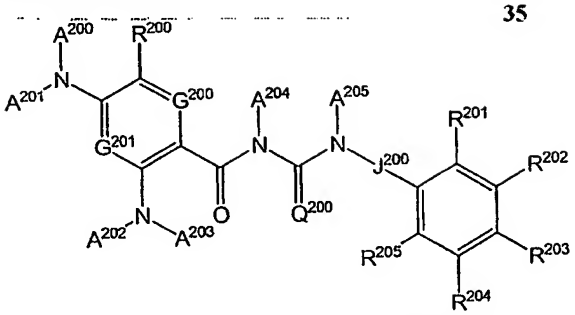
In an aspect of the invention an anti-fungal small molecule, analog or salt thereof has the following structure:



In an embodiment Ch^{190} is a chalcogen; and each of R^{190}, R^{191}, R^{192}, R^{193}, R^{194}, R^{195}, R^{196}, R^{197}, R^{198}, and R^{199} independently is one of –H, a halogen, an alkyl, –OH, or an alkoxy. In a second embodiment Ch^{190} is oxygen. In another embodiment at least one of R^{190}, R^{191}, R^{192}, R^{193}, R^{194}, or R^{195} is an alkyl. In a further embodiment at least two of R^{190}, R^{191}, R^{192}, R^{193}, R^{194}, or R^{195} independently is an alkyl. In yet another embodiment at least one of R^{190}, R^{191}, R^{192}, R^{193}, R^{194}, or R^{195} is methyl. In another embodiment each of R^{190} and R^{191} is methyl. In a further embodiment each of R^{192}, R^{193}, R^{194}, and R^{195} is –H. In yet another embodiment each of R^{196}, R^{197}, R^{198}, and R^{199} is –H. In a preferred embodiment the anti-fungal small molecule has the following structure:

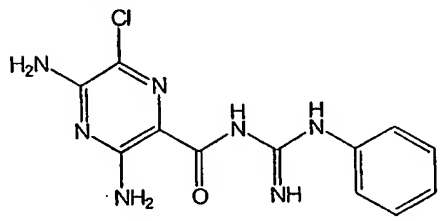


In an aspect of the invention an anti-fungal small molecule, analog or salt thereof has the following structure:

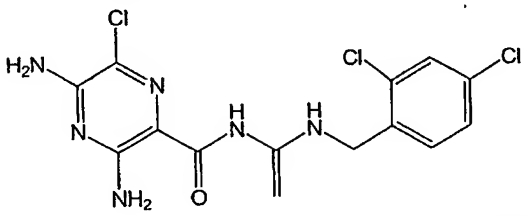


In an embodiment each of A^{200}, A^{201}, A^{202}, A^{203}, A^{204}, and A^{205} independently is one of –H or an alkyl; each of R^{200}, R^{201}, R^{202}, R^{203}, R^{204}, and R^{205} independently is one of –H, a halogen, an alkyl, –OH, or an alkoxy; each of G^{200} and G^{201} independently is one of N or CR, R being one of –H or an alkyl; Q^{200} is one of $=N-R^A$ or $=C(R^A)(R^B)$, each of R^A and R^B independently being one of –H or an alkyl; and J^{200} is one of a covalent bond or an alkyl. In a second embodiment at least one of A^{200} or A^{201} is –H. In another embodiment each of A^{200} and A^{201} is –H. In a further embodiment at least one of A^{202} or A^{203} is –H. In another embodiment each of A^{202} or A^{203} is –H. In an embodiment A^{204} is –H. In another embodiment A^{205} is –H. In a further embodiment R^{200} is a halogen. In yet another embodiment R^{200} is –Cl. In still another embodiment Q^{200} is $=C(R^A)(R^B)$. In a further embodiment Q^{200} is $=CH_2$. In still further embodiments Q^{200} is $=N-R^A$. In yet further embodiments Q^{200} is =NH.

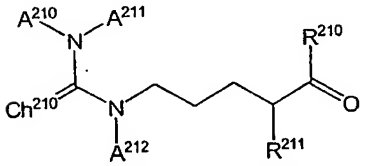
In an embodiment at least one of R^{201}, R^{202}, R^{203}, R^{204}, or R^{205} is a halogen. In a second embodiment at least two of R^{201}, R^{202}, R^{203}, R^{204}, or R^{205} independently is a halogen. In another embodiment at least one of R^{201}, R^{202}, R^{203}, R^{204}, or R^{205} is –Cl. In a further embodiment each of R^{201} and R^{203} is –Cl. In yet another embodiment each of R^{201}, R^{204}, and R^{205} is –H. In a further embodiment each of R^{201}, R^{202}, R^{203}, R^{204}, and R^{205} is –H. In still another embodiment at least one of G^{200} or G^{201} is N. In yet another embodiment each of G^{200} and G^{201} is N. In a further embodiment J^{200} is a covalent bond. In another embodiment J^{200} is an alkyl. In yet another embodiment J^{200} is $-CH_2-$. In a preferred embodiment the anti-fungal small molecule has the following structure:



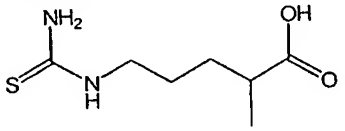
In aother preferred embodiment the anti-fungal small molecule has the following structure:



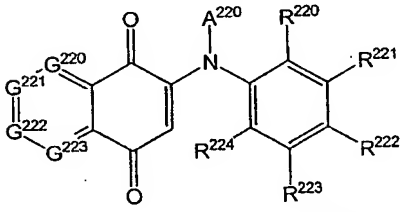
In an aspect of the invention an anti-fungal small molecule, analog or salt thereof has the following structure:



In an embodiment Ch^{210} is a chalcogen; each of A^{210}, A^{211}, and A^{212} independently is one of –H or an alkyl; and each of R^{210} and R^{211} independently is one of –H, a halogen, an alkyl, –OH, or an alkoxy. In a second embodiment Ch^{210} is sulfur. In another embodiment each of A^{210} and A^{211} is –H. In a further embodiment A^{212} is –H. In yet another embodiment R^{210} is –OH. In still another embodiment R^{211} is an alkyl. In another embodiment R^{211} is methyl. In a preferred embodiment the anti-fungal small molecule has the following structure:

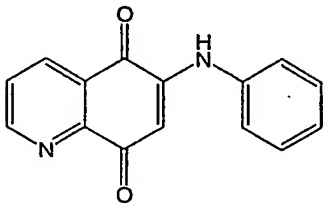


In an aspect of the invention an anti-fungal small molecule, analog or salt thereof has the following structure:

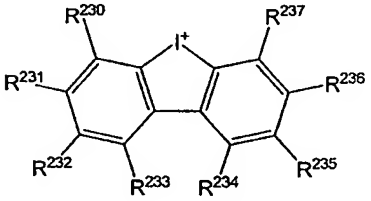


In an embodiment A^{220} is one of –H or an alkyl; each of R^{220}, R^{221}, R^{222}, R^{223}, and R^{224} independently is one of –H, a halogen, an alkyl, –OH, or an alkoxy; and each of G^{220}, G^{221}, G^{222}, and G^{223} independently is one of N or CR, R at each occurrence independently being one of –H or an alkyl. In a second embodiment A^{220} is –H. In another embodiment each of R^{220}, R^{221}, R^{222}, R^{223}, and R^{224} is –H. In a further embodiment at least one of G^{220}, G^{221}, G^{222}, or G^{223} is N. In yet another embodiment G^{223} is N. In still another embodiment

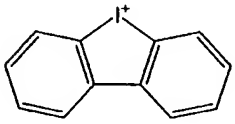
each of G^{220}, G^{221}, and G^{222} is –H. In a preferred embodiment the anti-fungal small molecule has the following structure:



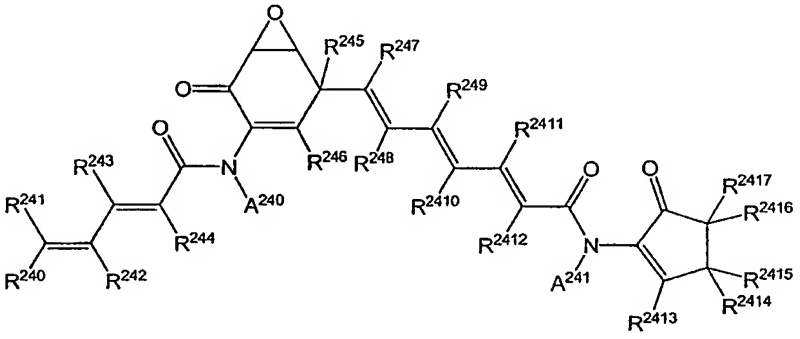
In an aspect of the invention an anti-fungal small molecule, analog or salt thereof has the following structure:



In an embodiment each of R^{230}, R^{231}, R^{232}, R^{233}, R^{234}, R^{235}, R^{236}, and R^{237} independently is one of –H, a halogen, an alkyl, –OH, or an alkoxy. In a second embodiment each of R^{230}, R^{231}, R^{232}, and R^{233} is –H. In another embodiment each of R^{234}, R^{235}, R^{236}, and R^{237} is –H. In a preferred embodiment the anti-fungal small molecule has the following structure:

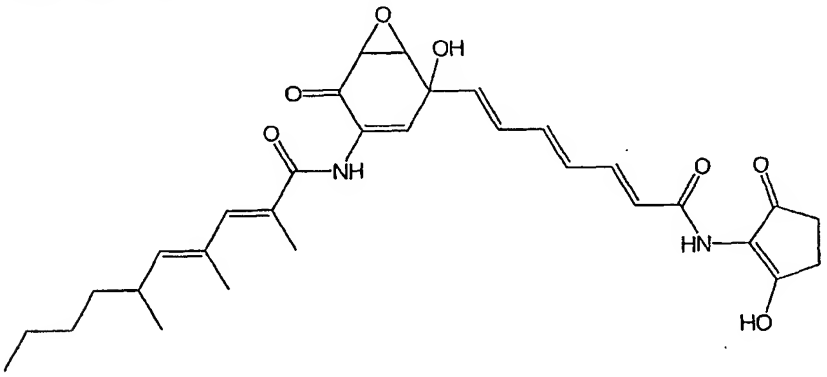


In an aspect of the invention an anti-fungal small molecule, analog or salt thereof has the following structure:

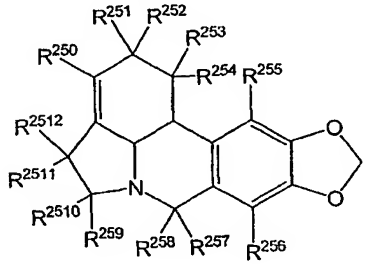


In an embodiment each of A^{240} and A^{241} independently is one of –H or an alkyl; and each of R^{240}, R^{241}, R^{242}, R^{243}, R^{244}, R^{245}, R^{246}, R^{247}, R^{248}, R^{249}, R^{2410}, R^{2411}, R^{2412}, R^{2413}, R^{2414}, R^{2415}, R^{2416}, and R^{2417} independently is one of –H, a halogen, an alkyl, –OH, or an alkoxy. In a second embodiment A^{240} is –H. In another embodiment A^{241} is –H. In a further

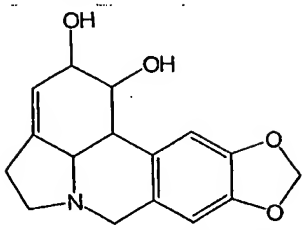
embodiment at least one of R^{240} or R^{241} is an alkyl. In yet another embodiment R^{240} is 1-methylpenytl. In still another embodiment R^{241} is –H. In another embodiment R^{242} is an alkyl. In a further embodiment R^{242} is methyl. In yet another embodiment R^{243} is –H. In still further embodiments R^{244} is an alkyl. In another embodiment R^{244} is methyl. In yet another embodiment R^{245} is –OH. In a further embodiment R^{246} is –H. In an embodiment each of R^{247}, R^{248}, R^{249}, R^{2410}, R^{2411}, and R^{2412} is –H. In another embodiment at least one of R^{2413}, R^{2414}, R^{2415}, R^{2416}, or R^{2417} is –OH. In a further embodiment R^{2413} is –OH. In yet another embodiment each of R^{2414}, R^{2415}, R^{2416}, and R^{2417} is –H. In a preferred embodiment the anti-fungal small molecule has the following structure:



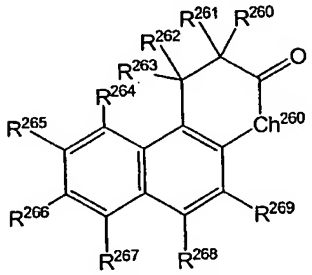
In an aspect of the invention an anti-fungal small molecule, analog or salt thereof has the following structure:



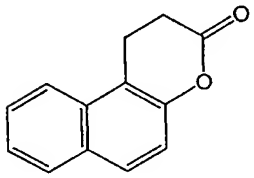
In an embodiment each of R^{250}, R^{251}, R^{252}, R^{253}, R^{254}, R^{255}, R^{256}, R^{257}, R^{258}, R^{259}, R^{2510}, R^{2511}, and R^{2512} independently is one of –H, a halogen, an alkyl, –OH, or an alkoxy. In a second embodiment at least one of R^{250}, R^{251}, R^{252}, R^{253}, or R^{254} is –OH. In another embodiment at least two of R^{250}, R^{251}, R^{252}, R^{253}, or R^{254} independently is –OH. In a further embodiment R^{251} is –OH. In yet another embodiment R^{253} is –OH. In still another embodiment each of R^{250}, R^{252}, and R^{254} is –H. In another embodiment each of R^{255} and R^{256} is –H. In a further embodiment each of R^{257} and R^{258} is –H. In yet another embodiment each of R^{259}, R^{2510}, R^{2511}, and R^{2512} is –H. In a preferred embodiment the anti-fungal small molecule has the following structure:



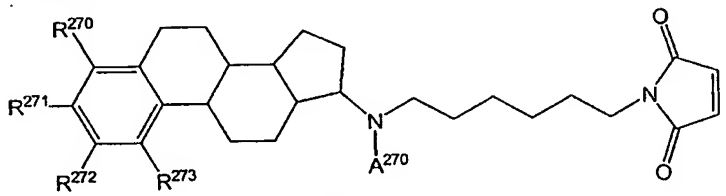
In an aspect of the invention an anti-fungal small molecule, analog or salt thereof has the following structure:



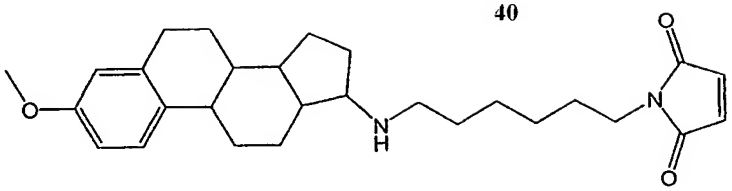
In an embodiment Ch^{260} is a chalcogen; and each of R^{260}, R^{261}, R^{262}, R^{263}, R^{264}, R^{265}, R^{266}, R^{267}, R^{268}, and R^{269} independently is one of –H, a halogen, an alkyl, –OH, or an alkoxy. In a second embodiment Ch^{260} is oxygen. In another embodiment each of R^{260}, R^{261}, R^{262}, and R^{263} is –H. In a further embodiment each of R^{264}, R^{265}, R^{266}, and R^{267} is –H. In yet another embodiment each of R^{268} and R^{269} is –H. In a preferred embodiment the anti-fungal small molecule has the following structure:



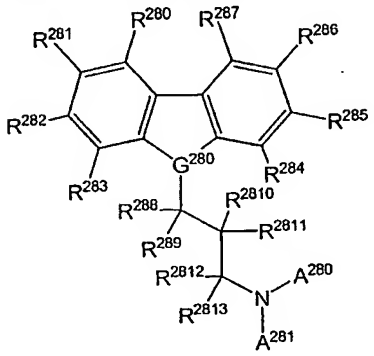
In an aspect of the invention an anti-fungal small molecule, analog or salt thereof has the following structure:



In an embodiment A^{270} is one of –H or an alkyl; and each of R^{270}, R^{271}, R^{272}, and R^{273} independently is one of –H, a halogen, an alkyl, –OH, or an alkoxy. In a second embodiment A^{270} is –H. In another embodiment at least one of R^{270}, R^{271}, R^{272}, or R^{273} is an alkoxy. In a further embodiment at least one of R^{270}, R^{271}, R^{272}, or R^{273} is methoxy. In yet another embodiment R^{271} is methoxy. In still another embodiment each of R^{270}, R^{272}, and R^{273} is –H. In a preferred embodiment the anti-fungal small molecule has the following structure:

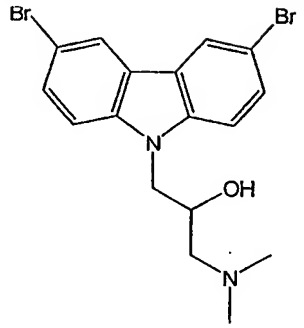


In an aspect of the invention an anti-fungal small molecule, analog or salt thereof has the following structure:

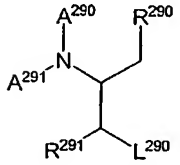


In an embodiment each of A^{280} and A^{281} independently is one of –H or an alkyl; each of R^{280}, R^{281}, R^{282}, R^{283}, R^{284}, R^{285}, R^{286}, R^{287}, R^{288}, R^{289}, R^{2810}, R^{2811}, R^{2812}, and R^{2813} independently is one of –H, a halogen, an alkyl, –OH, or an alkoxy; and G^{280} is one of N or CR, R being one of –H or an alkyl. In a second embodiment G^{280} is N. In another embodiment at least one of A^{280} or A^{281} is an alkyl. In a further embodiment each of A^{280} and A^{281} independently is an alkyl. In yet another embodiment at least one of A^{280} or A^{281} is methyl. In an embodiment each of A^{280} and A^{281} is methyl. In a further embodiment at least one of R^{280}, R^{281}, R^{282}, or R^{283} is a halogen. In a second embodiment at least one of R^{280}, R^{281}, R^{282}, or R^{283} is –Br. In another embodiment R^{281} is –Br. In a further embodiment each of R^{280}, R^{282}, and R^{283} is –H.

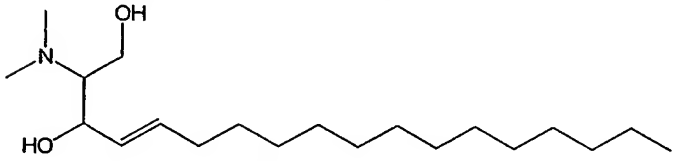
In an embodiment at least one of R^{284}, R^{285}, R^{286}, or R^{287} is a halogen. In a second embodiment at least one of R^{284}, R^{285}, R^{286}, or R^{287} is –Br. In another embodiment R^{286} is –Br. In a further embodiment each of R^{284}, R^{285}, and R^{287} is –H. In yet another embodiment R^{281} and R^{286} are identical. In still another embodiment at least one of R^{288}, R^{289}, R^{2810}, R^{2811}, R^{2812}, or R^{2813} is –OH. In another embodiment R^{2810} is –OH. In a further embodiment each of R^{288}, R^{289}, R^{2811}, R^{2812}, and R^{2813} is –H. In a preferred embodiment the anti-fungal small molecule has the following structure:



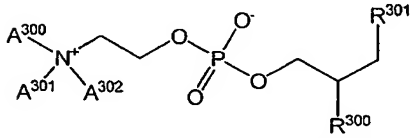
In an aspect of the invention an anti-fungal small molecule, analog or salt thereof has the following structure:



In an embodiment each of A^{290} and A^{291} independently is one of –H or an alkyl; L^{290} is an alkyl comprising at least 10 carbon atoms; and each of R^{290} and R^{291} independently is one of –H, a halogen, an alkyl, –OH, or an alkoxy. In a second embodiment at least one of A^{290} or A^{291} is an alkyl. In another embodiment each of A^{290} and A^{291} independently is an alkyl. In a further embodiment at least one of A^{290} or A^{291} is methyl. In yet another embodiment each of A^{290} and A^{291} is methyl. In an embodiment R^{290} is –OH. In another embodiment R^{291} is –OH. In an embodiment L^{290} comprises at least 12 carbon atoms. In another embodiment L^{290} comprises at least 15 carbon atoms. In a further embodiment L^{290} is a straight-chain alkyl. In yet another embodiment L^{290} is an alkenyl. In still another embodiment L^{290} is 1-pentadecenyl. In a preferred embodiment the anti-fungal small molecule has the following structure:

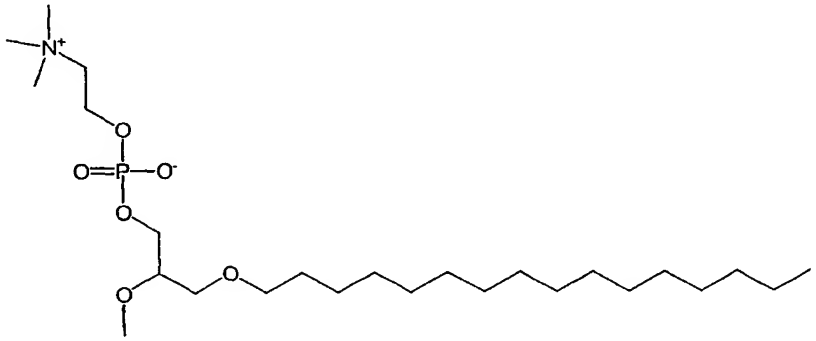


In an aspect of the invention an anti-fungal small molecule, analog or salt thereof has the following structure:

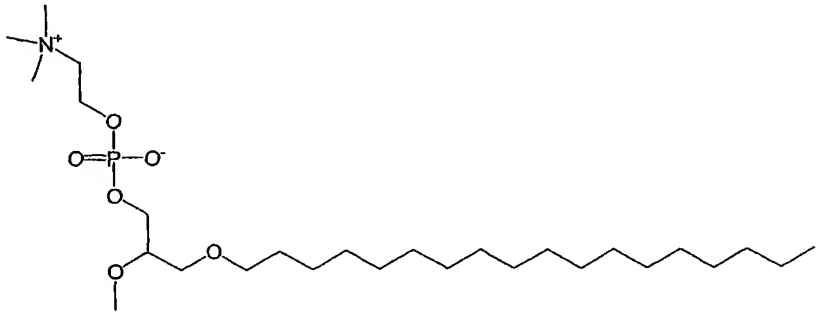


In an embodiment each of A^{300}, A^{301}, and A^{302} independently is one of –H or an alkyl; and each of R^{300} and R^{301} independently is one of –H, a halogen, an alkyl, –OH, or an alkoxy.

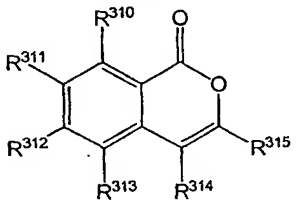
In a second embodiment at least one of A^{300}, A^{301}, or A^{302} is an alkyl. In another embodiment at least two of A^{300}, A^{301}, or A^{302} independently is an alkyl. In a further embodiment each of A^{300}, A^{301}, and A^{302} independently is an alkyl. In yet another embodiment at least one of A^{300}, A^{301}, or A^{302} is methyl. In still another embodiment each of A^{300}, A^{301}, and A^{302} is methyl. In an embodiment R^{300} is an alkoxy. In a second embodiment R^{300} is methoxy. In another embodiment R^{301} is an alkoxy. In a further embodiment R^{301} is an alkoxy comprising at least 10 carbon atoms. In yet another embodiment R^{301} comprises at least 12 carbon atoms. In still another embodiment R^{301} comprises at least 14 carbon atoms. In a further embodiment R^{301} comprises at least 16 carbon atoms. In still further embodiments R^{301} comprises at least 18 carbon atoms. In another embodiment R^{301} is a straight-chain alkoxy. In a further embodiment R^{301} is a saturated alkoxy. In yet another embodiment R^{301} is hexadecoxy. In a further embodiment R^{301} is octadecoxy. In a preferred embodiment the anti-fungal small molecule has the following structure:



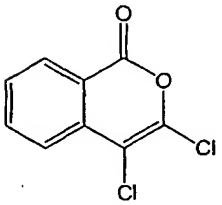
In another preferred embodiment the anti-fungal small molecule has the following structure:



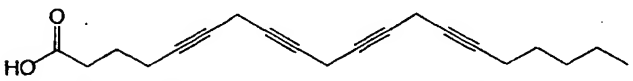
In an aspect of the invention an anti-fungal small molecule, analog or salt thereof has the following structure:



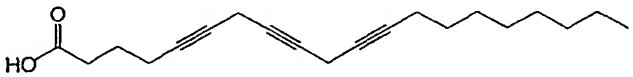
In an embodiment each of R^{310}, R^{311}, R^{312}, R^{313}, R^{314}, and R^{315} independently is one of –H, a halogen, an alkyl, –OH, or an alkoxy. In a second embodiment at least one of R^{310}, R^{311}, R^{312}, R^{313}, R^{314}, or R^{315} is a halogen. In another embodiment at least two of R^{310}, R^{311}, R^{312}, R^{313}, R^{314}, or R^{315} independently is a halogen. In a further embodiment at least one of R^{310}, R^{311}, R^{312}, R^{313}, R^{314}, or R^{315} is –Cl. In yet another embodiment each of R^{314} and R^{315} is –Cl. In still another embodiment each of R^{310}, R^{311}, R^{312}, and R^{313} is –H. In a preferred embodiment the anti-fungal small molecule has the following structure:



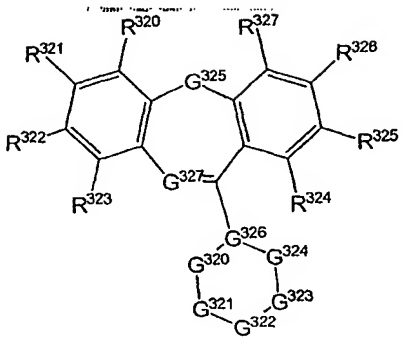
In an aspect of the invention an anti-fungal small molecule, analog or salt thereof is an alkanoic acid comprising at least 2 triple bonds. In an embodiment the alkanoic acid comprises at least 3 triple bonds. In a second embodiment the alkanoic acid comprises at least 4 triple bonds. In another embodiment the alkyl portion of the alkanoic acid is a straight-chain alkyl. In a further embodiment the alkyl comprises at least 6 carbon atoms. In yet another embodiment the alkyl comprises at least 8 carbon atoms. In still another embodiment the alkyl comprises at least 10 carbon atoms. In another embodiment the alkyl comprises at least 12 carbon atoms. In a further embodiment the alkyl comprises at least 14 carbon atoms. In yet another embodiment the alkyl comprises at least 16 carbon atoms. In still other embodiments the alkyl comprises at least 18 carbon atoms. In yet further embodiments the alkyl comprises at least 20 carbon atoms. In one preferred embodiment the anti-fungal small molecule has the following structure:



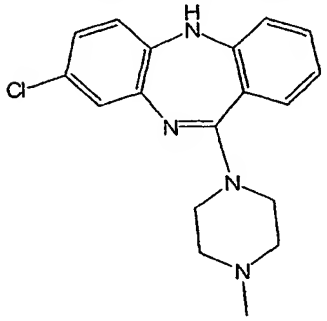
In another preferred embodiment the anti-fungal small molecule has the following structure:



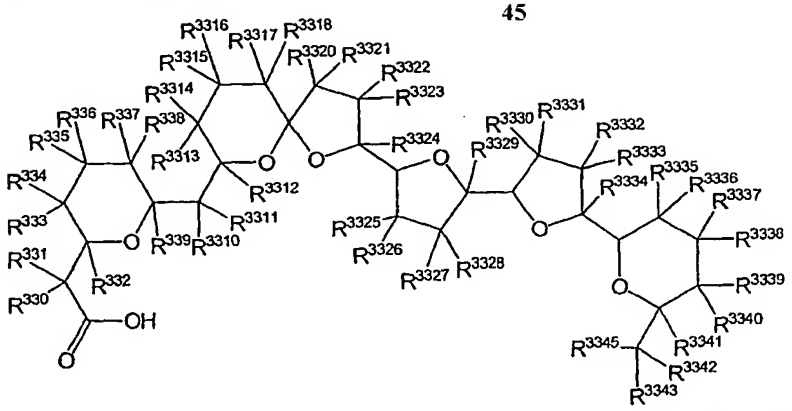
In an aspect of the invention an anti-fungal small molecule, analog or salt thereof has the following structure:



In an embodiment each of R^{320}, R^{321}, R^{322}, R^{323}, R^{324}, R^{325}, R^{326}, and R^{327} independently is one of –H, a halogen, an alkyl, –OH, or an alkoxy; each of G^{320}, G^{321}, G^{322}, G^{323}, G^{324}, and G^{325} independently is one of or  , R at each occurrence independently being one of –H or an alkyl; and each of G^{326} and G^{327} is independently one of N or CR, R at each occurrence independently being one of –H or an alkyl. In a second embodiment at least one of R^{320}, R^{321}, R^{322}, R^{323}, R^{324}, R^{325}, R^{326}, or R^{327} is a halogen. In another embodiment at least one of R^{320}, R^{321}, R^{322}, R^{323}, R^{324}, R^{325}, R^{326}, or R^{327} is –Cl. In a further embodiment R^{322} is –Cl. In yet another embodiment each of R^{320}, R^{321}, and R^{323} is –H. In still another embodiment each of R^{324}, R^{325}, R^{326}, and R^{327} is –H. In another embodiment G^{327} is N. In a further embodiment G^{325} is NH. In yet another embodiment G^{326} is N. In an embodiment at least one of G^{320}, G^{321}, G^{322}, G^{323}, or G^{324} is  . In another embodiment at least one of G^{320}, G^{321}, G^{322}, G^{323}, or G^{324} is  . In a further embodiment G^{322} is  . In yet another embodiment each of G^{320}, G^{321}, G^{323}, and G^{324} is  . In a preferred embodiment the anti-fungal small molecule has the following structure:



In an aspect of the invention an anti-fungal small molecule, analog or salt thereof has the following structure:

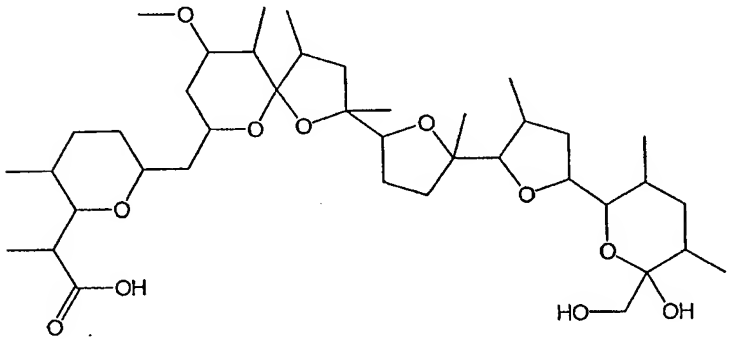


In an embodiment each of R^{330}, R^{331}, R^{332}, R^{333}, R^{334}, R^{335}, R^{336}, R^{337}, R^{338}, R^{339}, R^{3310}, R^{3311}, R^{3312}, R^{3313}, R^{3314}, R^{3315}, R^{3316}, R^{3317}, R^{3318}, R^{3319}, R^{3320}, R^{3321}, R^{3322}, R^{3323}, R^{3324}, R^{3325}, R^{3326}, R^{3327}, R^{3328}, R^{3329}, R^{3330}, R^{3331}, R^{3332}, R^{3333}, R^{3334}, R^{3335}, R^{3336}, R^{3337}, R^{3338}, R^{3339}, R^{3340}, R^{3341}, and R^{3342} independently is one of –H, a halogen, an alkyl, –OH, or an alkoxy. In a second embodiment R^{330} is an alkyl. In another embodiment R^{330} is methyl. In a further embodiment R^{331} is –H. In yet another embodiment R^{332} is –H. In an embodiment at least one of R^{333}, R^{334}, R^{335}, R^{336}, R^{337}, or R^{338} is an alkyl. In another embodiment at least one of R^{333}, R^{334}, R^{335}, R^{336}, R^{337}, or R^{338} is methyl. In a further embodiment R^{333} is methyl. In yet another embodiment each of R^{334}, R^{335}, R^{336}, R^{337}, and R^{338} is –H. In still another embodiment R^{339} is –H.

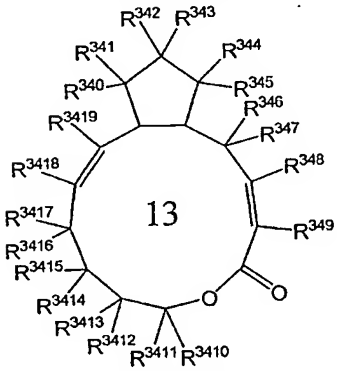
In an embodiment each of R^{3310} and R^{3311} is –H. In a second embodiment R^{3312} is –H. In another embodiment at least one of R^{3313}, R^{3314}, R^{3315}, R^{3316}, R^{3317}, or R^{3318} is an alkoxy. In a further embodiment at least one of R^{3313}, R^{3314}, R^{3315}, R^{3316}, R^{3317}, or R^{3318} is methoxy. In yet another embodiment R^{3315} is methoxy. In still another embodiment at least one of R^{3313}, R^{3314}, R^{3315}, R^{3316}, R^{3317}, or R^{3318} is an alkyl. In an embodiment at least one of R^{3313}, R^{3314}, R^{3315}, R^{3316}, R^{3317}, or R^{3318} is methyl. In another embodiment R^{3317} is methyl. In a further embodiment each of R^{3313}, R^{3314}, R^{3316}, and R^{3318} is –H. In yet another embodiment at least one of R^{3320}, R^{3321}, R^{3322}, or R^{3323} is an alkyl. In still another embodiment at least one of R^{3320}, R^{3321}, R^{3322}, or R^{3323} is methyl. In yet further embodiments R^{3320} is methyl.

In an embodiment each of R^{3321}, R^{3322}, and R^{3323} is –H. In a second embodiment R^{3324} is an alkyl. In another embodiment R^{3324} is methyl. In a further embodiment each of R^{3325}, R^{3326}, R^{3327}, and R^{3328} is –H. In yet another embodiment R^{3329} is an alkyl. In still another embodiment R^{3329} is methyl. In an embodiment at least one of R^{3330}, R^{3331}, R^{3332}, or R^{3333} is an alkyl. In another embodiment at least one of R^{3330}, R^{3331}, R^{3332}, or R^{3333} is methyl. In a further embodiment R^{3330} is methyl. In yet another embodiment each of R^{3331}, R^{3332}, and R^{3333} is –H. In still another embodiment R^{3334} is –H. In an embodiment at least one of R^{3335},

R^{3336}, R^{3337}, R^{3338}, R^{3339}, or R^{3340} is an alkyl. In another embodiment at least two of R^{3335}, R^{3336}, R^{3337}, R^{3338}, R^{3339}, or R^{3340} independently is an alkyl. In a further embodiment at least one of R^{3335}, R^{3336}, R^{3337}, R^{3338}, R^{3339}, or R^{3340} is methyl. In yet another embodiment each of R^{3335} and R^{3339} is methyl. In still another embodiment each of R^{3336}, R^{3337}, R^{3338}, and R^{3340} is –H. In a further embodiment R^{3341} is –OH. In another embodiment each of R^{3343} and R^{3344} is –H. In yet another embodiment R^{3345} is –OH. In a preferred embodiment the anti-fungal small molecule has the following structure:

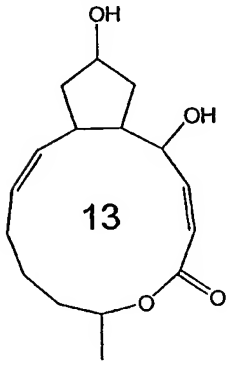


In an aspect of the invention an anti-fungal small molecule, analog or salt thereof has the following structure:

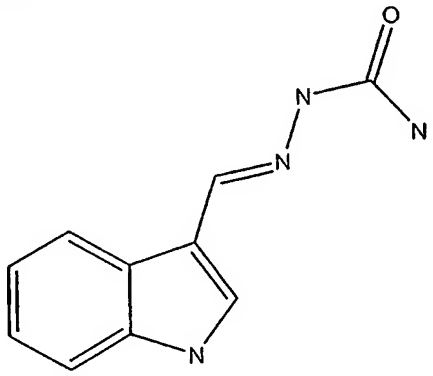


In an embodiment each of R^{340}, R^{341}, R^{342}, R^{343}, R^{344}, R^{345}, R^{346}, R^{347}, R^{348}, R^{349}, R^{3410}, R^{3411}, R^{3412}, R^{3413}, R^{3414}, R^{3415}, R^{3416}, R^{3417}, R^{3418}, and R^{3419} independently is one of –H, a halogen, an alkyl, –OH, or an alkoxy. In a second embodiment at least one of R^{340}, R^{341}, R^{342}, R^{343}, R^{344}, or R^{345} is –OH. In another embodiment R^{342} is –OH. In a further embodiment each of R^{340}, R^{341}, R^{343}, R^{344}, and R^{345} is –H. In yet another embodiment R^{346} is –OH. In still another embodiment R^{347} is –H. In an embodiment each of R^{348} and R^{349} is –H. In another embodiment at least one of R^{3410}, R^{3411}, R^{3412}, R^{3413}, R^{3414}, R^{3415}, R^{3416}, or R^{3417} is an alkyl. In a further embodiment at least one of R^{3410}, R^{3411}, R^{3412}, R^{3413}, R^{3414}, R^{3415}, R^{3416}, or R^{3417} is methyl. In yet another embodiment R^{3410} is methyl. In still another embodiment each of R^{3411}, R^{3412}, R^{3413}, R^{3414}, R^{3415}, R^{3416}, and R^{3417} is –H. In another embodiment each of

R^{3418} and R^{3419} is –H. In a preferred embodiment the anti-fungal small molecule has the following structure:



According to some aspects of the invention, the anti-fungal small molecules may be combined. In an embodiment of the invention the anti-fungal small molecule 4-(benzylidene-amino)-phenol may be combined with the anti-fungal small molecule 2-Chloro-5-nitro-N-phenylbenzamide analogs or salts thereof. In another embodiment of the invention the anti-fungal small molecule



may be combined with the anti-fungal small molecule 8-Chloro-11-(4-methyl-1-piperazinyl)-5H-dibenzo[b,e][1,4]-diazepine analogs or salts thereof. In a further embodiment of the invention the anti-fungal small molecule 1-(2-isopropyl-5-methyl-cyclohexyloxy)-3-piperidin-1-yl-propan-2-ol may be combined with the anti-fungal small molecule 8-Chloro-11-(4-methyl-1-piperazinyl)-5H-dibenzo[b,e][1,4]-diazepine analogs or salts thereof. In a further embodiment the anti fungal small molecule 4-(benzylidene-amino)-phenol may be combined with the anti-fungal small molecule 8-Chloro-11-(4-methyl-1-piperazinyl)-5H-dibenzo[b,e][1,4]-diazepine analogs or salts thereof. In another embodiment of the invention the anti-fungal small molecule 1-(2-isopropyl-5-methyl-cyclohexyloxy)-3-piperidin-1-yl-propan-2-ol may be combined with the anti-fungal small molecule 2-Chloro-5-nitro-N-phenylbenzamide analogs or salts thereof. In an embodiment of the invention the anti-fungal small molecule 4-(benzylidene-amino)-phenol may be combined with the anti-fungal small molecule ethyl [2-amino-6-bromo-4-(1-

cyano-2-ethoxy-2-oxoethyl)]-4H-chromene-3-carboxylate. It should be understood that any one or more of the anti-fungal small molecules of the invention may be combined with any other anti-fungal small molecule of the invention.

According to some aspects of the invention, the anti-fungal small molecules used in the methods for reducing the growth of a fungus or in the methods for treating fungal infection may exist in different isomeric forms. The anti-fungal small molecules may be used in the methods of the invention as a substantially isomerically-pure compound, or as a mixture of isomers. Preferably, isomerically-pure compounds are used. Isomerically-pure, as used herein, means that one isomer will be present in an amount ranging from 51 to 100%, preferably, more than 80%, more preferably, more than 90%, even more preferably, more than 95%, and even more preferably, more than 99% pure with respect to the other isomer or isomers present, but not with respect to other impurities or compounds that may be present. Isomer, as used herein, may refer to an *E* or *Z* isomer, and *R* or *S* isomer, an enantiomer, a diastereomer, or, in the case of anti-fungal small molecules with several diastereomers, a group of diastereomers, with respect to another group of diastereomers, which differ for example, with respect to just one stereocenter of the molecule.

As used herein, an "alkyl" is given its ordinary meaning as used in the field of organic chemistry. Alkyl or aliphatic groups typically contains any number of carbon atoms, for example, between 1 and 20 carbon atoms, between 1 and 15 carbon atoms, between 1 and 10 carbon atoms, or between 1 and 5 carbon atoms. In some embodiments, the alkyl group will contain at least 1 carbon atom, at least 2 carbon atoms, at least 3 carbon atoms, at least 4 carbon atoms, at least 5 carbon atoms, at least 6 carbon atoms, at least 7 carbon atoms, or at least 8 carbon atoms. Typically, an alkyl group is a non-cyclic structure. In certain embodiments, the alkyl group is a methyl group or an ethyl group.

The carbon atoms may be arranged in any configuration within the alkyl moiety, for example, as a straight chain (i.e., a *n*-alkyl such as methyl, ethyl, propyl, butyl, pentyl, hexyl, heptyl, octyl, nonyl, decyl, or undecyl) or a branched chain, for example, a *t*-butyl group, or an isoalkyl group such as isopropyl, isobutyl, ispentanyl, or isohexanyl. The alkyl moiety may contain none or any number of double or triple bonds within its structure, for example, as in an alkene, an alkyne, an alkadiene, an alkadiyne, an alkenyne, etc.

The alkyl group may contain any number of substituents. For example, the alkyl group may contain a halogen, an alkoxy (e.g., a methoxy, an ethoxy, a propoxy, an isopropoxy, a butoxy, a pentoxy, or the like), an amine (e.g., a primary, secondary, or tertiary amine, for example, an dimethylamine ethyl group), or a hydroxide as a substituent. As one

example, if the alkyl group is a methyl group, then the methyl group may be substituted to form, for instance, a halogenated methyl group such as chloromethyl, bromomethyl, or iodomethyl. In some embodiments of the invention, more than one substituent may be present. For example, the alkyl group may have two or more halogen atoms (for example, two chlorine atoms, or a chlorine and a bromine atom), a halogen and an alkoxy group, or the like.

In some embodiments of the invention, the alkyl group may also contain one or more heteroatoms substituted within the alkyl group, such as a nitrogen atom (e.g., as in an amine such as a primary, secondary, or tertiary amine) or an oxygen atom (as in an ether moiety). However, in other embodiments of the invention, the main chain of the alkyl group is free of heteroatoms and includes carbon atoms. As used herein, the term "heteroatoms" refers to atoms that can replace carbon atoms within an alkyl group without affecting the connectivity of the alkyl group; these typically include oxygen and nitrogen atoms. Halogen atoms and hydrogen atoms are not considered to be heteroatoms; for example, a chlorine atom can replace a hydrogen atom within an alkyl group without affecting the connectivity of the alkyl group As used herein, a "non-heteroatom alkyl group" is an alkyl group which does not contain any atoms at the carbon positions other than carbon. Some structures are defined as being free of non-terminal heteroatoms. As used herein, a "non-terminal" atom is an atom within a structure that is connected to at least two different atoms having a valency greater than 1 (e.g., the atom is connected to two non-hydrogen and non-halogen atoms). For example, the oxygen in $-CH_2-OH$ and the nitrogen atom in $-CH_2-NH_2$ are not connected to two different atoms having a valency greater than 1, and thus are not non-terminal heteroatoms.

The term "halogen," or equivalently, "halogen atom," is given its ordinary meaning as used in the field of chemistry. The halogens include fluorine, chlorine, bromine, iodine, and astatine. Preferably, the halogen atoms used in the present invention include one or more of fluorine, chlorine, bromine, or iodine. In certain embodiments of the invention, the halogen atoms found within the structure are fluorine, chlorine, and bromine; fluorine and chlorine; chlorine and bromine, or a single type of halogen atom.

In an aspect of the invention the anti-fungal small molecule is administered in an amount effective to reduce the growth of a fungus in a subject. As used herein an amount effective or effective amount, is an amount that is effective for producing some desired therapeutic effect in a subject at a reasonable benefit/risk ratio applicable to any medical treatment. An effective amount can mean an amount that reduces the symptoms in a subject

or reduces detectable levels of fungus. Accordingly, in some embodiments, an effective amount prevents or minimizes disease symptoms or progression associated with fungal infection or fungal growth. An effective amount can also prevent, delay, or reduce the growth of a fungus or the appearance of symptoms associated with the fungal growth.

Actual dosage levels of the active components in the anti-fungal small molecules of the invention may be varied so as to obtain an amount of the active component that is effective to achieve the desired therapeutic response for a particular patient, anti-fungal small molecule, and mode of administration, without being toxic to the patient. The selected dosage level will depend upon a variety of factors including the activity of the particular anti-fungal small molecule of the present invention employed, the route of administration, the time of administration, the rate of excretion or metabolism of the particular agent being employed, the duration of the treatment, other drugs, agents and/or materials used in combination with the particular anti-fungal small molecule employed, the age, gender, weight, condition, general health and prior medical history of the patient being treated, and like factors well known in the medical arts.

A physician or veterinarian having ordinary skill in the art can readily determine and prescribe the effective amount of the anti-fungal small molecule required. For example, the physician or veterinarian could start doses of the anti-fungal small molecule(s) of the invention employed in the pharmaceutical composition at levels lower than that required to achieve the desired therapeutic effect and then gradually increase the dosage until the desired effect is achieved.

In an aspect of the invention the anti-fungal small molecule may be administered by any means suitable to obtain the desired therapeutic effect. In one aspect the desired effect is the reduction of growth of a fungus. The anti-fungal small molecule in this case is administered in a suitable manner to reduce the growth of a fungus. Administration routes include but are not limited to parenteral administration, topical, oral, nasal, aerosol and enema. Parenteral administration includes but is not limited to subcutaneous, intravenous, intramuscular, intraperitoneal, and intrasternal injection, or infusion techniques. Oral routes include but are not limited to oral, nasal, dermal, sublingual and inhalants. In one embodiment the anti-fungal small molecule is administered as a topical lotion or other formulation.

In an aspect of the invention the anti-fungal small molecule is administered over a suitable period of time in order to reduce the growth of the fungus. Generally, daily doses of an anti-fungal small molecule will be from about 0.01 milligrams/kg per day to 1000

milligrams/kg per day. It is expected that oral doses in the range of 0.5 to 50 milligrams/kg, or even 1-10 milligrams/kg per day, in one or several administrations per day, will yield the desired results. Dosage may be adjusted appropriately to achieve desired drug levels, local or systemic, depending upon the mode of administration. For example, it is expected that intravenous administration would be from an order to several orders of magnitude lower dose per day. It is expected that intravenous and other parenteral forms of administration will yield the desired results in the range of 0.1 to 10 milligrams/kg per day. In the event that the response in a subject is insufficient at such doses, even higher doses (or effective higher doses by a different, more localized delivery route) may be employed to the extent that patient tolerance permits. Multiple doses per day are contemplated to achieve appropriate systemic levels of anti-fungal small molecules. When in a topical form it may be applied once, twice or multiple times a day as required. A long-term sustained release implant may be particularly suitable for the treatment of chronic conditions. "Long-term" release, as used herein, means that the implant is constructed and arranged to deliver therapeutic levels of the active ingredient for at least 7 days, and preferably 30-60 days. The implant may be positioned at the site of infection. Long-term sustained release implants are well-known to those of ordinary skill in the art.

In another aspect, the present invention provides "pharmaceutically acceptable" compositions, that include a therapeutically effective amount of one or more of the anti-fungal small molecules described herein, formulated together with one or more pharmaceutically acceptable carriers (additives) and/or diluents. The pharmaceutical compositions of the present invention may be specially formulated for administration in solid or liquid form, including those adapted for the following: oral administration, for example, drenches (aqueous or non-aqueous solutions or suspensions), tablets, e.g., those targeted for buccal, sublingual, and systemic absorption, boluses, powders, drops, granules, pastes for application to the tongue; parenteral administration, for example, by subcutaneous, intramuscular, intravenous or epidural injection as, for example, a sterile solution or suspension, or sustained-release formulation; topical application, for example, as a cream, ointment, drops, gels, or a controlled-release patch or spray applied to the skin, lungs, or oral cavity; intravaginally or intrarectally, for example, as a pessary, cream or foam; sublingually; ocularly; transdermally; or nasally, pulmonary and to other mucosal surfaces.

In one aspect of the invention topical lotion formulations are provided. A topical lotion comprises an anti-fungal small molecule and a topical carrier. Topical carriers include but are not limited to creams, ointments, drops, gels, or a controlled-release patch or spray

applied to the skin, lungs, or oral cavity. A topical carrier also includes a formulation administered intravaginally or intrarectally, for example, as a pessary, cream or foam, sublingually, ocularly, transdermally, or nasally, pulmonary, oralpharyngeal administration or to other mucosal surfaces. Suitable carrier components include, but are not limited to, mineral oil, sorbitan monostearate, polysorbate 60, cetyl esters wax, cetearyl alcohol, 2-octyldodecanol, benzyl alcohol, liquid petroleum, white petroleum, propylene glycol, polyoxyethylene polyoxypropylene compound, emulsifying wax and water.

The phrase "pharmaceutically acceptable" is employed herein to refer to those anti-fungal small molecules, materials, compositions, and/or dosage forms which are, within the scope of sound medical judgment, suitable for use in contact with the tissues of human beings and animals without excessive toxicity, irritation, allergic response, or other problem or complication, commensurate with a reasonable benefit/risk ratio.

The phrase "pharmaceutically-acceptable carrier" as used herein means a pharmaceutically-acceptable material, composition or vehicle, such as a liquid or solid filler, diluent, excipient, or solvent encapsulating material, involved in carrying or transporting the subject extract from one organ, or portion of the body, to another organ, or portion of the body. Each carrier must be "acceptable" in the sense of being compatible with the other ingredients of the formulation and not injurious to the patient. Some examples of materials which can serve as pharmaceutically-acceptable carriers include: sugars, such as lactose, glucose and sucrose; starches, such as corn starch and potato starch; cellulose, and its derivatives, such as sodium carboxymethyl cellulose, ethyl cellulose and cellulose acetate; powdered tragacanth; malt; gelatin; talc; excipients, such as cocoa butter and suppository waxes; oils, such as peanut oil, cottonseed oil, safflower oil, sesame oil, olive oil, corn oil and soybean oil; glycols, such as propylene glycol; polyols, such as glycerin, sorbitol, mannitol and polyethylene glycol; esters, such as ethyl oleate and ethyl laurate; agar; buffering agents, such as magnesium hydroxide and aluminum hydroxide; alginic acid; sterile distilled water; pyrogen-free water; isotonic saline; Ringer's solution; ethyl alcohol; pH buffered solutions; polyesters, polycarbonates and/or polyanhydrides; and other non-toxic compatible substances employed in pharmaceutical formulations.

Wetting agents, emulsifiers and lubricants, such as sodium lauryl sulfate and magnesium stearate, as well as coloring agents, release agents, coating agents, sweetening, flavoring and perfuming agents, preservatives and antioxidants can also be present in the compositions.

Examples of pharmaceutically-acceptable antioxidants include: water soluble antioxidants, such as ascorbic acid, cysteine hydrochloride, sodium bisulfate, sodium metabisulfite, sodium sulfite and the like; oil-soluble antioxidants, such as ascorbyl palmitate, butylated hydroxyanisole (BHA), butylated hydroxytoluene (BHT), lecithin, propyl gallate, alpha-tocopherol, and the like; and metal chelating agents, such as citric acid, ethylenediamine tetraacetic acid (EDTA), sorbitol, tartaric acid, phosphoric acid, and the like.

Formulations of the present invention include those suitable for oral, nasal, topical (including buccal and sublingual), rectal, vaginal and/or parenteral administration. The formulations may conveniently be presented in unit dosage form and may be prepared by any methods well known in the art of pharmacy. The amount of active component which can be combined with a carrier material to produce a single dosage form will vary depending upon the host being treated, and the particular mode of administration. The amount of active component that can be combined with a carrier material to produce a single dosage form will generally be that amount of the extract which produces a therapeutic effect. Generally, this amount will range from about 1% to about 99% of active component, preferably from about 5% to about 80%, most preferably from about 40% to about 60%.

In certain embodiments, a formulation of the present invention comprises an excipient selected from the group consisting of cyclodextrins, liposomes, micelle forming agents, e.g., bile acids, and polymeric carriers, e.g., polyesters and polyanhydrides; and an anti-fungal small molecule of the present invention.

The anti-fungal small molecules of the invention may optionally be delivered with other antifungal agents in the form of antifungal cocktails, or individually, yet close enough in time to have an effect on the treatment of the infection. An antifungal agent may be delivered simultaneously, concurrently or sequentially to an anti-fungal small molecule. An antifungal cocktail is a mixture of any one of the above-described anti-fungal small molecules with another antifungal drug which may or may not be an anti-fungal small molecule of the invention. The use of such cocktails in pharmaceutical preparations is routine. In an embodiment, a common administration vehicle (e.g. lotion, gel, tablet, implants, injectable solution, injectable liposome solution, etc.) could contain both the anti-fungal small molecule of the invention and the other antifungal agent(s). The anti-fungal agent in combination with an anti-fungal small molecule is delivered in an amount effective to reduce the growth of a fungus in a subject or to produce some other desired therapeutic effect as described herein. The anti-fungal agent either alone or in combination with an anti-fungal small molecule, may or may not be in an amount effective.

Antifungal agents include but are not limited to Acrisorcin; Ambruticin; Amphotericin B; Azaconazole; Azaserine; Basifungin; Bifonazole; Biphenamine Hydrochloride ; Bispyrithione Magsulfex ; Butoconazole Nitrate; Calcium Undecylenate; Candicidin; Carbol-Fuchsin; Chlordantoin; Ciclopirox; Ciclopirox Olamine; Cilofungin; Cisconazole; Clotrimazole; Cuprimyxin; Denofungin; Dipyrithione; Doconazole; Econazole; Econazole Nitrate; Enilconazole; Ethonam Nitrate; Fenticonazole Nitrate; Filipin; Fluconazole; Flucytosine; Fungimycin; Griseofulvin; Hamycin; Isoconazole; Itraconazole; Kalafungin; Ketoconazole; Lomofungin; Lydimycin; Mepartricin; Miconazole; Miconazole Nitrate; Monensin; Monensin Sodium; Naftifine Hydrochloride; Neomycin Undecylenate; Nifuratel; Nifurmerone; Nitralamine Hydrochloride; Nystatin; Octanoic Acid; Orconazole Nitrate; Oxiconazole Nitrate; Oxifungin Hydrochloride; Parconazole Hydrochloride; Partricin; Potassium Iodide; Proclonol; Pyrithione Zinc; Pyrrolnitrin; Rapamycin; Rutamycin; Sanguinarium Chloride; Saperconazole; Scopafungin; Selenium Sulfide; Sinefungin; Sulconazole Nitrate; Tamoxifen; Terbinafine; Terconazole; Thiram; Ticlatone ; Tioconazole; Tolciclate; Tolindate; Tolnaftate; Triacetin; Triafungin; Tunicamycin; Undecylenic Acid; Viridofulvin; Zinc Undecylenate; and Zinoconazole Hydrochloride.

Examples

Example 1

We provide numerous small molecules that inhibit either cell growth or the yeast-to-hyphal transition of the pathogenic yeast *Candida albicans*. These molecules have been identified from the ICCB/Harvard University Bioactive Knowns Collection. Analysis of the wide range of well-studied molecules in this collection has allowed us to systematically examine a variety of proteins and signaling pathways for their involvement in the budded-to-hyphal-form transition. For the screen, *C. albicans* cells were grown in YNB media that inhibits hyphal growth and then transferred to 384-well optical plates containing Spider media to induce the budded-to-hyphal transition and hyphal elongation. Next, small molecules were assayed for their ability to inhibit the Spider media-induced hyphal growth. Screening occurred on an inverted Nikon microscope with a computer driven XY stage with DIC/Hoffman optics, digital SPOT®camera and automatic shutter. Pictures were automatically taken of each well with the plate number and well position embedded in the picture through a script written for OpenLab® image analysis software from Improvision (INVIVO, from QED Imaging, Inc., Silver Spring, MD).

Using this strategy, we screened 490 molecules from the ICCB collection that have known biological functions and/or cellular targets. The small molecules were added at time 0 and growth was allowed to continue for 4 h at 37°C before the cells were fixed and observed microscopically. YNB media is well known in the art and contains yeast nitrogen base (DIFCO Labs., Detroit MI), glucose (US Biological, Swampscott, Massachusetts) and d-H_2O. Spider media is well known in the art and contains nutrient broth (DIFCO Labs., Detroit MI), mannitol (Sigma – Aldrich, St. Louis, MO), K_2HPO_4 (Sigma – Aldrich, St. Louis, MO) and d-H_2O.

Thirty nine of the screened molecules either inhibited *C. albicans* growth or inhibited the yeast-to-hyphal transition (Table 1). These molecules affected various signaling pathway components including those involved in Ca^{+2} function, transmembrane receptors, protein kinases, and others. These data implicate these molecules as anti-fungal drugs and their associated signaling pathways in the regulation of the budded-to-hyphal-form transition. In addition, several molecules (YC-1, L-744,832) have displayed potent anti-tumor activity. These exciting results indicate that we can use our robust and reproducible screen to identify molecules with known biological functions that can inhibit growth or the yeast-to-hyphal transition. These molecules, some of which are already FDA approved for other medical uses, are potential therapeutic molecules against lethal *C. albicans* infections.

Example 2

Cultures of *Candida albicans* were grown as described in Toenjes K. A. *et al.* (Antimicrobial Agents and Chemotherapy, 49(3):963-972, 2005). To induce hyphal growth, stationary-phase cultures were diluted into 5 ml of either YPD (1% yeast extract, 2% peptone, and 2% dextrose) plus 10% (vol/vol) fetal calf serum, Spider medium, Lee's medium (Lee, K. et al., Sabouraudia, 13:148-153, 1975), or M199 pH 8 medium (Sigma-Aldrich, St. Louis, MO) and grown at 37°C with shaking at 250 rpm.

Quantification of inhibition of the budded-to-hyphal-form transition was accomplished by counting the numbers of individual budded cells versus the number of hyphae in the population. More than 100 cells were counted for each assay in duplicate and all assays were repeated four times. Individual hyphae were counted as one cell, although the hyphae usually consisted of multiple individual hyphal cells. The percentage of hyphae reported was normalized to the percentage of hyphae formed when no molecule was added.

For the synergy assay, two different molecules (100 μM) were added together and the assay was performed in 10% serum media to induce hyphal formation.

Results: Table 2

Molecule added	% hyphae in 10% serum
235236	38%
GW9662	59%
235236 + GW9662	0%
235236	38%
Clozapine	33%
235236 + Clozapine	4%
105249	43%
HA14-1	34%
105249 + HA14-1	0%
121904	53%
Clozapine	33%
121904 + Clozapine	11%

Molecule 235236 showed a synergistic effect on hyphal growth in 10% serum with molecules GW9662 and Clozapine. Molecule 105249 showed a synergistic effect with HA14-1. Molecule 121904 showed a synergistic effect with Clozapine. Other combinations of molecules tested did not show synergistic effects on hyphal growth.

Table 1. Molecules that reduce fungal growth

Molecule	Presumed Mode of Action
TMB-8	Inhibits IP_3-induced intracellular Ca^{+2} release
Nigericin	K^+/H^+ exchanger; inhibits intracellular Ca^{+2} release
HA14-1	Bcl-2 inhibitor; induces apoptosis and Ca^{+2} release
Tyrphostin AG1478	EGF receptor tyrosine kinase inhibitor
Tyrphostin 9	PDGF receptor tyrosine kinase inhibitor
Clozapine	Dopamine receptor antagonist
Fluspiriline	Dopamine receptor antagonist
GW-9662	Peroxisome proliferator-activated receptor (PPARγ) antagonist
YC-1	NO-independent guanylyl cyclase activator; anti-tumor activity
L-744,832	Peptidomimetic farnesyltransferase inhibitor
GW-5074	Inhibitor of Raf-1 phosphorylation
5,8,11,14-eicosatetraynoic acid	Prostaglandin and leukotriene antagonist
Penitrem A (tremortin A)	Large conductance Ca^{+2} activated maxi-K channel blocker
SKF-96365	Receptor mediated and voltage-gated Ca^{+2} channel blocker
TPEN	Heavy metal chelator; low affinity for Ca^{+2} and Mg^{+2}
AG213 (Tyrphostin 47)	EGF receptor kinase inhibitor
Calyculin A	Protein phosphatase 1 and 2A inhibitor
Ro 31-8220	Protein kinase inhibitor
K252A	Protein kinase inhibitor
ML-7	Protein kinase inhibitor
ML-9	Protein kinase inhibitor
BAY 11-7082	Inhibits TNF-α-inducible phosphorylation of IκB-α
RK-682	Protein tyrosine phosphatase inhibitor
Beta-lapachone	DNA topoisomerase I inhibitor
Dichlorobenzamil	8-Br-cGMP inhibitor
Thiocitrulline	Inhibitor of constitutive nitric oxide (NO) synthase
LY-83583	Inhibits NO-induced activation of soluble guanylyl cyclase C
Diphenyleneiodonium Cl	Endothelial nitric oxide synthase (eNOS) inhibitor
Manumycin A	Inhibits farnesyltransferase
Lycorine	Peptidyl transferase inhibitor
Brefeldin A	Inhibits protein translocation
Phenamil	Amiloride-sensitive sodium channel inhibitor
Splitomycin	Inhibitor of histone deacetylase activity of Sir2 protein
U73122	Inhibits agonist-induced phospholipase C activation
Wiskostatin	Inhibits actin filament assembly; inhibitor of N-WASP
N,N-dimethylsphingosine	Bioactive lipid
1-hexadecyl-2-methylglycero-3 phosphatidylcholine	Bioactive lipid
3,4-dichloroisocoumarin	Inhibitor of multiple enzyme targets; factor D inhibitor
5,8,11-eicosatriynoic acid	5-LO, 12-LO, 15-LO and cyclooxygenase inhibitor

The foregoing written specification is considered to be sufficient to enable one skilled in the art to practice the invention. The present invention is not to be limited in scope by examples provided, since the examples are intended as a single illustration of one aspect of the invention and other functionally equivalent embodiments are within the scope of the invention. Various modifications of the invention in addition to those shown and described herein will become apparent to those skilled in the art from the foregoing description and fall within the scope of the appended claims. The advantages and objects of the invention are not necessarily encompassed by each embodiment of the invention. Those skilled in the art will recognize, or be able to ascertain using no more than routine experimentation, many equivalents to the specific embodiments of the invention described herein. Such equivalents are intended to be encompassed by the following claims.

All references disclosed herein are incorporated by reference in their entirety.

We claim:

Claims

1. A method for reducing growth of a fungus comprising

contacting a fungal cell with an anti-fungal small molecule in an amount effective to reduce the growth of the fungal cell, wherein the anti-fungal small molecule is one or more of the following 8-(N,N-Diethylamino)-octyl-3,4,5-trimethoxybenzoate HCl, Ethyl [2-amino-6-bromo-4-(1-cyano-2-ethoxy-2-oxoethyl)]-4H-chromene-3-carboxylate, N-(3-Chlorophenyl)-6,7-dimethoxy-4-quinazolinamine, [[3,5-bis(1,1-Dimethylethyl)-4-hydroxyphenyl]methylene]propanedinitrile, 8-Chloro-11-(4-methyl-1-piperazinyl)-5H-dibenzo[b,e][1,4]-diazepine, 8-[4,4-bis(p-Fluorophenyl)butyl]-1-phenyl-1,3,8-triazino[4.5]decan-4-one, 2-Chloro-5-nitro-N-phenylbenzamide, 3-(5'-Hydroxymethyl-2'-furyl)-1-benzylindazole, (2S)-2-[[(2S)-2-[(2S,3S)-2-[(2R)-2-Amino-3-mercaptopropyl]amino]-3-methylpentyl]oxy]-1-oxo-3-phenylpropyl]amino]-4-(methylsulfonyl)-butanoic Acid 1-Methylethyl Ester, 3-(3,5-Dibromo-4-hydroxybenzyliden)-5-iodo-1,2-dihydroindol-2-one, 5,8,11,14-eicosatetrayonic acid, *Penicillium palitans* Penitrem A, 1-[β-[3-(4-Methoxyphenyl)propoxy]-4-methoxyphenethyl]-1H-imidazole HCl, N,N,N',N'-*tetrakis*-(2-pyridylmethyl)-ethylenediamine, 3,4-Dihydroxy-a-cyanothiocinnamamide a-Cyano-3,4-dihydroxythiocinnamamide, *Discodermia calyx* Calyculin A, 3-[1-[3-(Amidinothio)propyl-1H-indol-3-yl]-3-(1-methyl-1H-indol-3-yl)maleimide Bisindolylmaleimide IX Methanesulfonate, *Nocardiopsis* K252A, 1-(5-Iodonapthalene-1-sulfonyl)homopiperazine, 1-(5-Chloronapthalene-1-sulfonyl)homopiperazine HCl, *Streptomyces hygroscopicus* Nigericin, γ,4-Dihydroxy-2-(6-hydroxy-1-heptenyl)-4-cyclopentanecrotonic acidλ-lactone, (E)3-[(4-Methylphenyl)sulfonyl]-2-propenenitrile, 3-Hexadecanoyl-5-hydroxymethyl-tetronic Acid, *Tabebuia avellanedae* Beta-lapachone, 2,4-Dichlorobenzamil, 2-Thioureido-L-norvaline, 6-Anilino-5,8-quinolinequinone, Diphenyleneiodonium Cl, Manumycin A, Lycorine, 3,5-Diamino-6-chloro-N-[imino(phenylamino)methyl]pyrazinecarboxamide, 1,2-Dihydro-3H-naphtho[2,1-b]pyran-3-one, 1-(6-(17β-3-methoxyestra-1,3,5(10)-trien-17-yl)amino)hexyl)-1H-pyrrole-2,5-dione, 1-(3,6-Dibromocarbazol-9-yl)-3-dimethylaminopropan-2-ol, N_1N-dimethylsphingosine, 1-hexadecyl-2-methylglycero-3-phosphatidylcholine, 1-octadecyl-2-methylglycero-3-phosphatidylcholine, 3,4-dichloroisocoumarin, or 5,8,11-eicosatriyonic acid, 4-(benzylidene-amino)-phenol, or 1-(2-isopropyl-5-methyl-cyclohexyloxy)-3-piperidin-1-yl-propan-2-ol, or analogs or salts thereof.

2. The method of claim 2, wherein the method is a method for treating a subject having or at risk of having a fungal infection further comprising administering the anti-fungal small molecule to the subject.

3. The method of claim 2, wherein the fungal cell is selected from the group consisting of *Candida albicans*, *Pneumocystis carinii*, *Saccharomyces cerevisiae*, *Aspergillus nidulans*, *Kluyveromyces lactis*, *Schizosaccharomyces pombe*, *Streptomyces lasaliensis*, *Streptomyces hygroscopicus*, *Candida tropicalis*, *Candida dubliniensis*, *Candida parapsilosis*, *Candida kefyr*, *Candida guilliermondii*, *Candida inconspicua*, *Candida famata*, *Candida glabrata*, *Candida krusei*, *Candida lusitaniae*, *Cryptococcus neoformans*, *Coccidioides immitis*, and *Hispolasma capsulatum*.

4. The method of claim 2, wherein the fungal cell is a pathogenic yeast.

5. The method of claim 4, wherein the pathogenic yeast is *Candida albicans*.

6. The method of claim 2, wherein the anti-fungal small molecule is 8-(N,N-Diethylamino)-octyl-3,4,5-trimethoxybenzoate HCl, 8-(N,N-Diethylamino)-octyl-3,4,5-trimethoxybenzoate HCl analogs or salts thereof.

7. The method of claim 2, wherein the anti-fungal small molecule is Ethyl [2-amino-6-bromo-4-(1-cyano-2-ethoxy-2-oxoethyl)]-4H-chromene-3-carboxylate, Ethyl [2-amino-6-bromo-4-(1-cyano-2-ethoxy-2-oxoethyl)]-4H-chromene-3-carboxylate analogs or salts thereof.

8. The method of claim 2, wherein the anti-fungal small molecule is N-(3-Chlorophenyl)-6,7-dimethoxy-4-quinazolinamine, N-(3-Chlorophenyl)-6,7-dimethoxy-4-quinazolinamine analogs or salts thereof.

9. The method of claim 2, wherein the anti-fungal small molecule is [[3,5-bis(1,1-Dimethylethyl)-4-hydroxyphenyl]methylene]propanedinitrile, [[3,5-bis(1,1-Dimethylethyl)-4-hydroxyphenyl]methylene]propanedinitrile analogs or salts thereof.

10. The method of claim 2, wherein the anti-fungal small molecule is 8-Chloro-11-(4-methyl-1-piperazinyl)-5H-dibenzo[b,e][1,4]-diazepine, 8-Chloro-11-(4-methyl-1-piperazinyl)-5H-dibenzo[b,e][1,4]-diazepine analogs or salts thereof.

11. The method of claim 2, wherein the anti-fungal small molecule is 8-[4,4-bis(p-Fluorophenyl)butyl]-1-phenyl-1,3,8-triazino[4.5]decan-4-one, 8-[4,4-bis(p-Fluorophenyl)butyl]-1-phenyl-1,3,8-triazino[4.5]decan-4-one analogs or salts thereof.

12. The method of claim 2, wherein the anti-fungal small molecule is 2-Chloro-5-nitro-N-phenylbenzamide, 2-Chloro-5-nitro-N-phenylbenzamide analogs or salts thereof.

13. The method of claim 2, wherein the anti-fungal small molecule is 3-(5'-Hydroxymethyl-2'-furyl)-1-benzylindazole, 3-(5'-Hydroxymethyl-2'-furyl)-1-benzylindazole analogs or salts thereof.

14. The method of claim 2, wherein the anti-fungal small molecule is (2S)-2-[[(2S)-2-[(2S,3S)-2-[(2R)-2-Amino-3-mercaptopropyl]amino]-3-methylpentyl]oxy]-1-oxo-3-phenylpropyl]amino]-4-(methylsulfonyl)-butanoic Acid 1-Methylethyl Ester, (2S)-2-[[(2S)-2-[(2S,3S)-2-[(2R)-2-Amino-3-mercaptopropyl]amino]-3-methylpentyl]oxy]-1-oxo-3-phenylpropyl]amino]-4-(methylsulfonyl)-butanoic Acid 1-Methylethyl Ester analogs or salts thereof.

15. The method of claim 2, wherein the anti-fungal small molecule is 3-(3,5-Dibromo-4-hydroxybenzyliden)-5-iodo-1,2-dihydroindol-2-one, 3-(3,5-Dibromo-4-hydroxybenzyliden)-5-iodo-1,2-dihydroindol-2-one analogs or salts thereof.

16. The method of claim 2, wherein the anti-fungal small molecule is 5,8,11,14-eicosatetrayonic acid, 5,8,11,14-eicosatetrayonic acid analogs or salts thereof.

17. The method of claim 2, wherein the anti-fungal small molecule is *Penicillium palitans* Penitrem A, *Penicillium palitans* Penitrem A analogs or salts thereof.

18. The method of claim 2, wherein the anti-fungal small molecule is 1-[β-[3-(4-Methoxyphenyl)propoxy]-4-methoxyphenethyl]-1H-imidazole HCl, 1-[β-[3-(4-Methoxyphenyl)propoxy]-4-methoxyphenethyl]-1H-imidazole HCl analogs or salts thereof.

19. The method of claim 2, wherein the anti-fungal small molecule is N,N,N',N'-*tetrakis*-(2-pyridylmethyl)-ethylenediamine, N,N,N',N'-*tetrakis*-(2-pyridylmethyl)-ethylenediamine analogs or salts thereof.

20. The method of claim 2, wherein the anti-fungal small molecule is 3,4-Dihydroxy-a-cyanothiocinnamamide a-Cyano-3,4-dihydroxythiocinnamamide, 3,4-Dihydroxy-a-cyanothiocinnamamide a-Cyano-3,4-dihydroxythiocinnamamide analogs or salts thereof.

21. The method of claim 2, wherein the anti-fungal small molecule is *Discodermia calyx* Calyculin A, *Discodermia calyx* Calyculin A analogs or salts thereof.

22. The method of claim 2, wherein the anti-fungal small molecule is 3-[1-[3-(Amidinothio)propyl-1H-indol-3-yl]-3-(1-methyl-1H-indol-3-yl)maleimide Bisindolylmaleimide IX Methanesulfonate, 3-[1-[3-(Amidinothio)propyl-1H-indol-3-yl]-3-(1-methyl-1H-indol-3-yl)maleimide Bisindolylmaleimide IX Methanesulfonate analogs or salts thereof.

23. The method of claim 2, wherein the anti-fungal small molecule is *Nocardiopsis* K252A, *Nocardiopsis* K252A analogs or salts thereof.

24. The method of claim 2, wherein the anti-fungal small molecule is 1-(5-Iodonapthalene-1-sulfonyl)homopiperazine, 1-(5-Iodonapthalene-1-sulfonyl)homopiperazine analogs or salts thereof.

25. The method of claim 2, wherein the anti-fungal small molecule is 1-(5-Chloronapthalene-1-sulfonyl)homopiperazine HCl, 1-(5-Chloronapthalene-1-sulfonyl)homopiperazine HCl analogs or salts thereof.

26. The method of claim 2, wherein the anti-fungal small molecule is (E)3-[(4-Methylphenyl)sulfonyl]-2-propenenitrile, (E)3-[(4-Methylphenyl)sulfonyl]-2-propenenitrile analogs or salts thereof.

27. The method of claim 2, wherein the anti-fungal small molecule is 3-Hexadecanoyl-5-hydroxymethyl-tetronic Acid, 3-Hexadecanoyl-5-hydroxymethyl-tetronic Acid analogs or salts thereof.

28. The method of claim 2, wherein the anti-fungal small molecule is *Tabebuia avellanedae* Beta-lapachone, *Tabebuia avellanedae* Beta-lapachone analogs or salts thereof.

29. The method of claim 2, wherein the anti-fungal small molecule is 2,4-Dichlorobenzamil, 2,4-Dichlorobenzamil analogs or salts thereof.

30. The method of claim 2, wherein the anti-fungal small molecule is 2-Thioureido-L-norvaline, 2-Thioureido-L-norvaline analogs or salts thereof.

31. The method of claim 2, wherein the anti-fungal small molecule is 6-Anilino-5,8-quinolinequinone, 6-Anilino-5,8-quinolinequinone analogs or salts thereof.

32. The method of claim 2, wherein the anti-fungal small molecule is Diphenyleneiodonium Cl, Diphenyleneiodonium Cl analogs or salts thereof.

33. The method of claim 2, wherein the anti-fungal small molecule is Manumycin A, Manumycin A analogs or salts thereof.

34. The method of claim 2, wherein the anti-fungal small molecule is Lycorine, Lycorine analogs or salts thereof.

35. The method of claim 2, wherein the anti-fungal small molecule is 3,5-Diamino-6-chloro-N-[imino(phenylamino)methyl]pyrazinecarboxamide, 3,5-Diamino-6-chloro-N-[imino(phenylamino)methyl]pyrazinecarboxamide analogs or salts thereof.

36. The method of claim 2, wherein the anti-fungal small molecule is 1,2-Dihydro-3H-naphtho[2,1-b]pyran-3-one, 1,2-Dihydro-3H-naphtho[2,1-b]pyran-3-one analogs or salts thereof.

37. The method of claim 2, wherein the anti-fungal small molecule is 1-(6-(17β-3-methoxyestra-1,3,5(10)-trien-17-yl)amino)hexyl)-1H-pyrrole-2,5-dione, 1-(6-(17β-3-methoxyestra-1,3,5(10)-trien-17-yl)amino)hexyl)-1H-pyrrole-2,5-dione analogs or salts thereof.

38. The method of claim 2, wherein the anti-fungal small molecule is 1-(3,6-Dibromocarbazol-9-yl)-3-dimethylaminopropan-2-ol, 1-(3,6-Dibromocarbazol-9-yl)-3-dimethylaminopropan-2-ol analogs or salts thereof.

39. The method of claim 2, wherein the anti-fungal small molecule is N_1N-dimethylsphingosine, N_1N-dimethylsphingosine analogs or salts thereof.

40. The method of claim 2, wherein the anti-fungal small molecule is 1-hexadecyl-2-methylglycero-3-phosphatidylcholine, 1-hexadecyl-2-methylglycero-3-phosphatidylcholine analogs or salts thereof.

41. The method of claim 2, wherein the anti-fungal small molecule is 1-octadecyl-2-methylglycero-3-phosphatidylcholine, 1-octadecyl-2-methylglycero-3-phosphatidylcholine analogs or salts thereof.

42. The method of claim 2, wherein the anti-fungal small molecule is 3,4-dichloroisocoumarin, 3,4-dichloroisocoumarin analogs or salts thereof.

43. The method of claim 2, wherein the anti-fungal small molecule is 5,8,11-eicosatriyonic acid, 5,8,11-eicosatriyonic acid analogs or salts thereof.

44. The method of claim 2, wherein the anti-fungal small molecule is *Streptomyces hygroscopicus* Nigericin, *Streptomyces hygroscopicus* Nigericin analogs or salts thereof.

45. The method of claim 2, wherein the anti-fungal small molecule is γ,4-Dihydroxy-2-(6-hydroxy-1-heptenyl)-4-cyclopentanecrotonic acidλ-lactone, γ,4-Dihydroxy-2-(6-hydroxy-1-heptenyl)-4-cyclopentanecrotonic acidλ-lactone analogs or salts thereof.

46. The method of claim 2, wherein the fungal infection is a pathogenic yeast.

47. The method of claim 46, wherein the fungal infection is *Candida albicans*.

48. The method of claim 2, wherein the subject is a human.

49. The method of claim 2, wherein the subject is immunocompromised.

50. The method of claim 2, wherein the subject has had chemotherapy.

51. The method of claim 2, wherein the subject has AIDS.

52. The method of claim 2, wherein the subject has had a transplant.

53. The method of claim 2, wherein the subject has a central venous catheter.

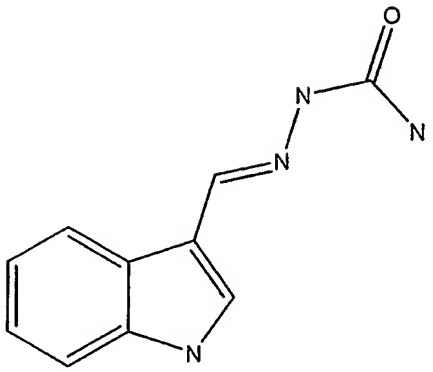
54. The method of claim 2, wherein the anti-fungal small molecule is administered via injection, topical route, oral route, nasal route, aerosol, or enema route.

55. The method of claim 2, wherein the anti-fungal small molecule is administered via an oral route.

56. The method of claim 2, wherein the anti-fungal small molecule is administered via a topical route.

57. The method of claim 2, wherein the anti-fungal small molecule is 4-(benzylidene-amino)-phenol and 2-Chloro-5-nitro-N-phenylbenzamide analogs or salts thereof.

58. The method of claim 2, wherein the anti-fungal small molecule is



and 8-Chloro-11-(4-methyl-1-piperazinyl)-5H-dibenzo[b,e][1,4]-diazepine analogs or salts thereof.

59. The method of claim 2, wherein the anti-fungal small molecule is 1-(2-isopropyl-5-methyl-cyclohexyloxy)-3-piperidin-1-yl-propan-2-ol and 8-Chloro-11-(4-methyl-1-piperazinyl)-5H-dibenzo[b,e][1,4]-diazepine analogs or salts thereof.

60. The method of claim 2, wherein the anti-fungal small molecule is 4-(benzylidene-amino)-phenol and ethyl [2-amino-6-bromo-4-(1-cyano-2-ethoxy-2-oxoethyl)]-4H-chromene-3-carboxylate analogs or salts thereof.

61. A composition comprising

an anti-fungal small molecule and an anti-fungal agent, wherein the anti-fungal small molecule is one or more of the following 8-(N,N-Diethylamino)-octyl-3,4,5-trimethoxybenzoate HCl, Ethyl [2-amino-6-bromo-4-(1-cyano-2-ethoxy-2-oxoethyl)]-4H-chromene-3-carboxylate, N-(3-Chlorophenyl)-6,7-dimethoxy-4-quinazolinamine, [[3,5-bis(1,1-Dimethylethyl)-4-hydroxyphenyl]methylene]propanedinitrile, 8-Chloro-11-(4-methyl-1-piperazinyl)-5H-dibenzo[b,e][1,4]-diazepine, 8-[4,4-bis(p-Fluorophenyl)butyl]-1-phenyl-1,3,8-triazino[4.5]decan-4-one, 2-Chloro-5-nitro-N-phenylbenzamide, 3-(5'-Hydroxymethyl-2'-furyl)-1-benzylindazole, (2S)-2-[[(2S)-2-[(2S,3S)-2-[(2R)-2-Amino-3-mercaptopropyl]amino]-3-methylpentyl]oxy]-1-oxo-3-phenylpropyl]amino]-4-(methylsulfonyl)-butanoic Acid 1-Methylethyl Ester, 3-(3,5-Dibromo-4-hydroxybenzyliden)-5-iodo-1,2-dihydroindol-2-one, 5,8,11,14-eicosatetrayonic acid, *Penicillium palitans* Penitrem A, 1-[β-[3-(4-Methoxyphenyl)propoxy]-4-methoxyphenethyl]-1H-imidazole HCl, N,N,N',N'-*tetrakis*-(2-pyridylmethyl)-ethylenediamine, 3,4-Dihydroxy-a-cyanothiocinnamamide a-Cyano-3,4-dihydroxythiocinnamamide, *Discodermia calyx*

Calyculin A, 3-[1-[3-(Amidinothio)propyl-1H-indol-3-yl]-3-(1-methyl-1H-indol-3-yl)maleimide Bisindolylmaleimide IX Methanesulfonate, *Nocardiopsis* K252A, 1-(5-Iodonapthalene-1-sulfonyl)homopiperazine, 1-(5-Chloronapthalene-1-sulfonyl)homopiperazine HCl, *Streptomyces hygroscopicus* Nigericin, γ,4-Dihydroxy-2-(6-hydroxy-1-heptenyl)-4-cyclopentanecrotonic acidλ-lactone, (E)3-[(4-Methylphenyl)sulfonyl]-2-propenenitrile, 3-Hexadecanoyl-5-hydroxymethyl-tetronic Acid, *Tabebuia avellanedae* Beta-lapachone, 2,4-Dichlorobenzamil, 2-Thioureido-L-norvaline, 6-Anilino-5,8-quinolinequinone, Diphenyleneiodonium Cl, Manumycin A, Lycorine, 3,5-Diamino-6-chloro-N-[imino(phenylamino)methyl]pyrazinecarboxamide, 1,2-Dihydro-3H-naphtho[2,1-b]pyran-3-one, 1-(6-(17β-3-methoxyestra-1,3,5(10)-trien-17-yl)amino)hexyl)-1H-pyrrole-2,5-dione, 1-(3,6-Dibromocarbazol-9-yl)-3-dimethylaminopropan-2-ol, N_1N-dimethylsphingosine, 1-hexadecyl-2-methylglycero-3-phosphatidylcholine, 1-octadecyl-2-methylglycero-3-phosphatidylcholine, 3,4-dichloroisocoumarin, or 5,8,11-eicosatriyonic acid, 4-(benzylidene-amino)-phenol, or 1-(2-isopropyl-5-methyl-cyclohexyloxy)-3-piperidin-1-yl-propan-2-ol, or analogs or salts thereof.

62. The composition of claim 61, wherein the anti-fungal agent is an anti-*Candida albicans* agent.

63. The composition of claim 62, wherein the anti-*Candida albicans* agent is selected from the group consisting of Acrisorcin; Ambruticin; Amphotericin B; Azaconazole; Azaserine; Basifungin; Bifonazole; Biphenamine Hydrochloride ; Bispyrithione Magsulfex ; Butoconazole Nitrate; Calcium Undecylenate; Candicidin; Carbol-Fuchsin; Chlordantoin; Ciclopirox; Ciclopirox Olamine; Cilofungin; Cisconazole; Clotrimazole; Cuprimyxin; Denofungin ; Dipyrithione; Doconazole; Econazole; Econazole Nitrate; Enilconazole; Ethonam Nitrate; Fenticonazole Nitrate; Filipin; Fluconazole; Flucytosine; Fungimycin; Griseofulvin; Hamycin; Isoconazole ; Itraconazole; Kalafungin; Ketoconazole; Lomofungin; Lydimycin; Mepartricin ; Miconazole; Miconazole Nitrate; Monensin ; Monensin Sodium ; Naftifine Hydrochloride; Neomycin Undecylenate ; Nifuratel ; Nifurmerone; Nitralamine Hydrochloride; Nystatin; Octanoic Acid; Orconazole Nitrate; Oxiconazole Nitrate; Oxifungin Hydrochloride; Parconazole Hydrochloride; Partricin ; Potassium Iodide ; Proclonol ; Pyrithione Zinc ; Pyrrolnitrin; Rapamycin; Rutamycin; Sanguinarium Chloride ; Saperconazole; Scopafungin ; Selenium Sulfide ; Sinefungin; Sulconazole Nitrate; Tamoxifen; Terbinafine; Terconazole; Thiram; Ticlatone ; Tioconazole; Tolciclate;

Tolindate; Tolnaftate; Triacetin; Triafungin; Tunicamycin; Undecylenic Acid; Viridofulvin; Zinc Undecylenate; and Zinoconazole Hydrochloride.

64. The composition of claim 61, wherein the anti-fungal small molecule is 8-(N,N-Diethylamino)-octyl-3,4,5-trimethoxybenzoate HCl, 8-(N,N-Diethylamino)-octyl-3,4,5-trimethoxybenzoate HCl analogs or salts thereof.

65. The composition of claim 61, wherein the anti-fungal small molecule is Ethyl [2-amino-6-bromo-4-(1-cyano-2-ethoxy-2-oxoethyl)]-4H-chromene-3-carboxylate, Ethyl [2-amino-6-bromo-4-(1-cyano-2-ethoxy-2-oxoethyl)]-4H-chromene-3-carboxylate analogs or salts thereof.

66. The composition of claim 61, wherein the anti-fungal small molecule is N-(3-Chlorophenyl)-6,7-dimethoxy-4-quinazolinamine, N-(3-Chlorophenyl)-6,7-dimethoxy-4-quinazolinamine analogs or salts thereof.

67. The composition of claim 61, wherein the anti-fungal small molecule is [[3,5-bis(1,1-Dimethylethyl)-4-hydroxyphenyl]methylene]propanedinitrile, [[3,5-bis(1,1-Dimethylethyl)-4-hydroxyphenyl]methylene]propanedinitrile analogs or salts thereof.

68. The composition of claim 61, wherein the anti-fungal small molecule is 8-Chloro-11-(4-methyl-1-piperazinyl)-5H-dibenzo[b,e][1,4]-diazepine, 8-Chloro-11-(4-methyl-1-piperazinyl)-5H-dibenzo[b,e][1,4]-diazepine analogs or salts thereof.

69. The composition of claim 61, wherein the anti-fungal small molecule is 8-[4,4-bis(p-Fluorophenyl)butyl]-1-phenyl-1,3,8-triazino[4.5]decan-4-one, 8-[4,4-bis(p-Fluorophenyl)butyl]-1-phenyl-1,3,8-triazino[4.5]decan-4-one analogs or salts thereof.

70. The composition of claim 61, wherein the anti-fungal small molecule is 2-Chloro-5-nitro-N-phenylbenzamide, 2-Chloro-5-nitro-N-phenylbenzamide analogs or salts thereof.

71. The composition of claim 61, wherein the anti-fungal small molecule is 3-(5'-Hydroxymethyl-2'-furyl)-1-benzylindazole, 3-(5'-Hydroxymethyl-2'-furyl)-1-benzylindazole analogs or salts thereof.

72. The composition of claim 61, wherein the anti-fungal small molecule is (2S)-2-[[(2S)-2-[(2S,3S)-2-[(2R)-2-Amino-3-mercaptopropyl]amino]-3-methylpentyl]oxy]-1-oxo-3-phenylpropyl]amino]-4-(methylsulfonyl)-butanoic Acid 1-Methylethyl Ester, (2S)-2-[[(2S)-2-[(2S,3S)-2-[(2R)-2-Amino-3-mercaptopropyl]amino]-3-methylpentyl]oxy]-1-oxo-3-phenylpropyl]amino]-4-(methylsulfonyl)-butanoic Acid 1-Methylethyl Ester analogs or salts thereof.

73. The composition of claim 61, wherein the anti-fungal small molecule is 3-(3,5-Dibromo-4-hydroxybenzyliden)-5-iodo-1,2-dihydroindol-2-one, 3-(3,5-Dibromo-4-hydroxybenzyliden)-5-iodo-1,2-dihydroindol-2-one analogs or salts thereof.

74. The composition of claim 61, wherein the anti-fungal small molecule is 5,8,11,14-eicosatetrayonic acid, 5,8,11,14-eicosatetrayonic acid analogs or salts thereof.

75. The composition of claim 61, wherein the anti-fungal small molecule is *Penicillium palitans* Penitrem A, Penitrem A analogs or salts thereof.

76. The composition of claim 61, wherein the anti-fungal small molecule is 1-[β-[3-(4-Methoxyphenyl)propoxy]-4-methoxyphenethyl]-1H-imidazole HCl, 1-[β-[3-(4-Methoxyphenyl)propoxy]-4-methoxyphenethyl]-1H-imidazole HCl analogs or salts thereof.

77. The composition of claim 61, wherein the anti-fungal small molecule is N,N,N',N'-*tetrakis*-(2-pyridylmethyl)-ethylenediamine, N,N,N',N'-*tetrakis*-(2-pyridylmethyl)-ethylenediamine analogs or salts thereof.

78. The composition of claim 61, wherein the anti-fungal small molecule is 3,4-Dihydroxy-a-cyanothiocinnamamide a-Cyano-3,4-dihydroxythiocinnamamide, 3,4-Dihydroxy-a-cyanothiocinnamamide a-Cyano-3,4-dihydroxythiocinnamamide analogs or salts thereof.

79. The composition of claim 61, wherein the anti-fungal small molecule is *Discodermia calyx* Calyculin A, *Discodermia calyx* Calyculin A analogs or salts thereof.

80. The composition of claim 61, wherein the anti-fungal small molecule is 3-[1-[3-(Amidinothio)propyl-1H-indol-3-yl]-3-(1-methyl-1H-indol-3-yl)maleimide Bisindolylmaleimide IX Methanesulfonate, 3-[1-[3-(Amidinothio)propyl-1H-indol-3-yl]-3-(1-methyl-1H-indol-3-yl)maleimide Bisindolylmaleimide IX Methanesulfonate analogs or salts thereof.

81. The composition of claim 61, wherein the anti-fungal small molecule is *Nocardiopsis* K252A, *Nocardiopsis* K252A analogs or salts thereof.

82. The composition of claim 61, wherein the anti-fungal small molecule is 1-(5-Iodonapthalene-1-sulfonyl)homopiperazine, 1-(5-Iodonapthalene-1-sulfonyl)homopiperazine analogs or salts thereof.

83. The composition of claim 61, wherein the anti-fungal small molecule is 1-(5-Chloronapthalene-1-sulfonyl)homopiperazine HCl, 1-(5-Chloronapthalene-1-sulfonyl)homopiperazine HCl analogs or salts thereof.

84. The composition of claim 61, wherein the anti-fungal small molecule is (E)3-[(4-Methylphenyl)sulfonyl]-2-propenenitrile, (E)3-[(4-Methylphenyl)sulfonyl]-2-propenenitrile analogs or salts thereof.

85. The composition of claim 61, wherein the anti-fungal small molecule is 3-Hexadecanoyl-5-hydroxymethyl-tetronic Acid, 3-Hexadecanoyl-5-hydroxymethyl-tetronic Acid analogs or salts thereof.

86. The composition of claim 61, wherein the anti-fungal small molecule is *Tabebuia avellanedae* Beta-lapachone, *Tabebuia avellanedae* Beta-lapachone analogs or salts thereof.

87. The composition of claim 61, wherein the anti-fungal small molecule is 2,4-Dichlorobenzamil, 2,4-Dichlorobenzamil analogs or salts thereof.

88. The composition of claim 61, wherein the anti-fungal small molecule is 2-Thioureido-L-norvaline, 2-Thioureido-L-norvaline analogs or salts thereof.

89. The composition of claim 61, wherein the anti-fungal small molecule is 6-Anilino-5,8-quinolinequinone, 6-Anilino-5,8-quinolinequinone analogs or salts thereof.

90. The composition of claim 61, wherein the anti-fungal small molecule is Diphenyleneiodonium Cl, Diphenyleneiodonium Cl analogs or salts thereof.

91. The composition of claim 61, wherein the anti-fungal small molecule is Manumycin A, Manumycin A analogs or salts thereof.

92. The composition of claim 61, wherein the anti-fungal small molecule is Lycorine, Lycorine analogs or salts thereof.

93. The composition of claim 61, wherein the anti-fungal small molecule is 3,5-Diamino-6-chloro-N-[imino(phenylamino)methyl]pyrazinecarboxamide, 3,5-Diamino-6-chloro-N-[imino(phenylamino)methyl]pyrazinecarboxamide analogs or salts thereof.

94. The composition of claim 61, wherein the anti-fungal small molecule is 1,2-Dihydro-3H-naphtho[2,1-b]pyran-3-one, 1,2-Dihydro-3H-naphtho[2,1-b]pyran-3-one analogs or salts thereof.

95. The composition of claim 61, wherein the anti-fungal small molecule is 1-(6-(17β-3-methoxyestra-1,3,5(10)-trien-17-yl)amino)hexyl)-1H-pyrrole-2,5-dione, 1-(6-(17β-3-methoxyestra-1,3,5(10)-trien-17-yl)amino)hexyl)-1H-pyrrole-2,5-dione analogs or salts thereof.

96. The composition of claim 61, wherein the anti-fungal small molecule is 1-(3,6-Dibromocarbazol-9-yl)-3-dimethylaminopropan-2-ol, 1-(3,6-Dibromocarbazol-9-yl)-3-dimethylaminopropan-2-ol analogs or salts thereof.

97. The composition of claim 61, wherein the anti-fungal small molecule is N_1N-dimethylsphingosine, N_1N-dimethylsphingosine analogs or salts thereof.

98. The composition of claim 61, wherein the anti-fungal small molecule is 1-hexadecyl-2-methylglycero-3-phosphatidylcholine, 1-hexadecyl-2-methylglycero-3-phosphatidylcholine analogs or salts thereof.

99. The composition of claim 61, wherein the anti-fungal small molecule is 1-octadecyl-2-methylglycero-3-phosphatidylcholine, 1-octadecyl-2-methylglycero-3-phosphatidylcholine analogs or salts thereof.

100. The composition of claim 61, wherein the anti-fungal small molecule is 3,4-dichloroisocoumarin, 3,4-dichloroisocoumarin analogs or salts thereof.

101. The composition of claim 61, wherein the anti-fungal small molecule is 5,8,11-eicosatriyonic acid, 5,8,11-eicosatriyonic acid analogs or salts thereof.

102. The composition of claim 61, wherein the anti-fungal small molecule is *Streptomyces hygroscopicus* Nigericin, Nigericin analogs or salts thereof.

103. The composition of claim 61, wherein the anti-fungal small molecule is γ,4-Dihydroxy-2-(6-hydroxy-1-heptenyl)-4-cyclopentanecrotonic acidλ-lactone, γ,4-Dihydroxy-2-(6-hydroxy-1-heptenyl)-4-cyclopentanecrotonic acidλ-lactone analogs or salts thereof.

104. The composition of claim 61, wherein the anti-fungal agent is selected from the group consisting of Acrisorcin; Ambruticin; Amphotericin B; Azaconazole; Azaserine; Basifungin; Bifonazole; Biphenamine Hydrochloride; Bispyrithione Magsulfex; Butoconazole Nitrate; Calcium Undecylenate; Candicidin; Carbol-Fuchsin; Chlordantoin; Ciclopirox; Ciclopirox Olamine; Cilofungin; Cisconazole; Clotrimazole; Cuprimyxin; Denofungin; Dipyrithione; Doconazole; Econazole; Econazole Nitrate; Enilconazole; Ethonam Nitrate; Fenticonazole Nitrate; Filipin; Fluconazole; Flucytosine; Fungimycin; Griseofulvin; Hamycin; Isoconazole ; Itraconazole; Kalafungin; Ketoconazole; Lomofungin; Lydimycin; Mepartricin; Miconazole; Miconazole Nitrate; Monensin; Monensin Sodium; Naftifine Hydrochloride; Neomycin Undecylenate; Nifuratel; Nifurmerone; Nitralamine Hydrochloride; Nystatin; Octanoic Acid; Orconazole Nitrate; Oxiconazole Nitrate; Oxifungin Hydrochloride; Parconazole Hydrochloride; Partricin; Potassium Iodide; Proclonol; Pyrithione Zinc; Pyrrolnitrin; Rapamycin; Rutamycin; Sanguinarium Chloride; Saperconazole; Scopafungin; Selenium

Sulfide; Sinefungin; Sulconazole Nitrate; Tamoxifen; Terbinafine; Terconazole; Thiram; Ticlatone; Tioconazole; Tolciclate; Tolindate; Tolnaftate; Triacetin; Triafungin; Tunicamycin; Undecylenic Acid; Viridofulvin; Zinc Undecylenate; and Zinoconazole Hydrochloride.

105. A topical lotion comprising

an anti-fungal small molecule and a topical carrier, wherein the anti-fungal small molecule is one or more of the following 8-(N,N-Diethylamino)-octyl-3,4,5-trimethoxybenzoate HCl, Ethyl [2-amino-6-bromo-4-(1-cyano-2-ethoxy-2-oxoethyl)]-4H-chromene-3-carboxylate, N-(3-Chlorophenyl)-6,7-dimethoxy-4-quinazolinamine, [[3,5-bis(1,1-Dimethylethyl)-4-hydroxyphenyl]methylene]propanedinitrile, 8-Chloro-11-(4-methyl-1-piperazinyl)-5H-dibenzo[b,e][1,4]-diazepine, 8-[4,4-bis(p-Fluorophenyl)butyl]-1-phenyl-1,3,8-triazino[4.5]decan-4-one, 2-Chloro-5-nitro-N-phenylbenzamide, 3-(5'-Hydroxymethyl-2'-furyl)-1-benzylindazole, (2S)-2-[[(2S)-2-[(2S,3S)-2-[(2R)-2-Amino-3-mercaptopropyl]amino]-3-methylpentyl]oxy]-1-oxo-3-phenylpropyl]amino]-4-(methylsulfonyl)-butanoic Acid 1-Methylethyl Ester, 3-(3,5-Dibromo-4-hydroxybenzyliden)-5-iodo-1,2-dihydroindol-2-one, 5,8,11,14-eicosatetrayonic acid, *Penicillium palitans* Penitrem A, 1-[β-[3-(4-Methoxyphenyl)propoxy]-4-methoxyphenethyl]-1H-imidazole HCl, N,N,N',N'-*tetrakis*-(2-pyridylmethyl)-ethylenediamine, 3,4-Dihydroxy-a-cyanothiocinnamamide a-Cyano-3,4-dihydroxythiocinnamamide, *Discodermia calyx* Calyculin A, 3-[1-[3-(Amidinothio)propyl-1H-indol-3-yl]-3-(1-methyl-1H-indol-3-yl)maleimide Bisindolylmaleimide IX Methanesulfonate, *Nocardiopsis* K252A, 1-(5-Iodonapthalene-1-sulfonyl)homopiperazine, 1-(5-Chloronapthalene-1-sulfonyl)homopiperazine HCl, *Streptomyces hygroscopicus* Nigericin, γ,4-Dihydroxy-2-(6-hydroxy-1-heptenyl)-4-cyclopentanecrotonic acidλ-lactone, (E)3-[(4-Methylphenyl)sulfonyl]-2-propenenitrile, 3-Hexadecanoyl-5-hydroxymethyl-tetronic Acid, *Tabebuia avellanedae* Beta-lapachone, 2,4-Dichlorobenzamil, 2-Thioureido-L-norvaline, 6-Anilino-5,8-quinolinequinone, Diphenyleneiodonium Cl, Manumycin A, Lycorine, 3,5-Diamino-6-chloro-N-[imino(phenylamino)methyl]pyrazinecarboxamide, 1,2-Dihydro-3H-naphtho[2,1-b]pyran-3-one, 1-(6-(17β-3-methoxyestra-1,3,5(10)-trien-17-yl)amino)hexyl)-1H-pyrrole-2,5-dione, 1-(3,6-Dibromocarbazol-9-yl)-3-dimethylaminopropan-2-ol, N_1N-dimethylsphingosine, 1-hexadecyl-2-methylglycero-3-phosphatidylcholine, 1-octadecyl-2-methylglycero-3-phosphatidylcholine, 3,4-dichloroisocoumarin, 5,8,11-eicosatriyonic acid, 4-

(benzylidene-amino)-phenol, or 1-(2-isopropyl-5-methyl-cyclohexyloxy)-3-piperidin-1-yl-propan-2-ol, or analogs or salts thereof.

106. The topical lotion of claim 105, wherein the anti-fungal small molecule is 8-(N,N-Diethylamino)-octyl-3,4,5-trimethoxybenzoate HCl, 8-(N,N-Diethylamino)-octyl-3,4,5-trimethoxybenzoate HCl analogs or salts thereof.

107. The topical lotion of claim 105, wherein the anti-fungal small molecule is Ethyl [2-amino-6-bromo-4-(1-cyano-2-ethoxy-2-oxoethyl)]-4H-chromene-3-carboxylate, Ethyl [2-amino-6-bromo-4-(1-cyano-2-ethoxy-2-oxoethyl)]-4H-chromene-3-carboxylate analogs or salts thereof.

108. The topical lotion of claim 105, wherein the anti-fungal small molecule is N-(3-Chlorophenyl)-6,7-dimethoxy-4-quinazolinamine, N-(3-Chlorophenyl)-6,7-dimethoxy-4-quinazolinamine analogs or salts thereof.

109. The topical lotion of claim 105, wherein the anti-fungal small molecule is [[3,5-bis(1,1-Dimethylethyl)-4-hydroxyphenyl]methylene]propanedinitrile, [[3,5-bis(1,1-Dimethylethyl)-4-hydroxyphenyl]methylene]propanedinitrile analogs or salts thereof.

110. The topical lotion of claim 105, wherein the anti-fungal small molecule is 8-Chloro-11-(4-methyl-1-piperazinyl)-5H-dibenzo[b,e][1,4]-diazepine, 8-Chloro-11-(4-methyl-1-piperazinyl)-5H-dibenzo[b,e][1,4]-diazepine analogs or salts thereof.

111. The topical lotion of claim 105, wherein the anti-fungal small molecule is 8-[4,4-bis(p-Fluorophenyl)butyl]-1-phenyl-1,3,8-triazino[4.5]decan-4-one, 8-[4,4-bis(p-Fluorophenyl)butyl]-1-phenyl-1,3,8-triazino[4.5]decan-4-one analogs or salts thereof.

112. The topical lotion of claim 105, wherein the anti-fungal small molecule is 2-Chloro-5-nitro-N-phenylbenzamide, 2-Chloro-5-nitro-N-phenylbenzamide analogs or salts thereof.

113. The topical lotion of claim 105, wherein the anti-fungal small molecule is 3-(5'-Hydroxymethyl-2'-furyl)-1-benzylindazole, 3-(5'-Hydroxymethyl-2'-furyl)-1-benzylindazole analogs or salts thereof.

114. The topical lotion of claim 105, wherein the anti-fungal small molecule is (2S)-2-[[(2S)-2-[(2S,3S)-2-[(2R)-2-Amino-3-mercaptopropyl]amino]-3-methylpentyl]oxy]-1-oxo-3-phenylpropyl]amino]-4-(methylsulfonyl)-butanoic Acid 1-Methylethyl Ester, (2S)-2-[[(2S)-2-[(2S,3S)-2-[(2R)-2-Amino-3-mercaptopropyl]amino]-3-methylpentyl]oxy]-1-oxo-3-phenylpropyl]amino]-4-(methylsulfonyl)-butanoic Acid 1-Methylethyl Ester analogs or salts thereof.

115. The topical lotion of claim 105, wherein the anti-fungal small molecule is 3-(3,5-Dibromo-4-hydroxybenzyliden)-5-iodo-1,2-dihydroindol-2-one, 3-(3,5-Dibromo-4-hydroxybenzyliden)-5-iodo-1,2-dihydroindol-2-one analogs or salts thereof.

116. The topical lotion of claim 105, wherein the anti-fungal small molecule is 5,8,11,14-eicosatetrayonic acid, 5,8,11,14-eicosatetrayonic acid analogs or salts thereof.

117. The topical lotion of claim 105, wherein the anti-fungal small molecule is *Penicillium palitans* Penitrem A, *Penicillium palitans* Penitrem A analogs or salts thereof.

118. The topical lotion of claim 105, wherein the anti-fungal small molecule is 1-[β-[3-(4-Methoxyphenyl)propoxy]-4-methoxyphenethyl]-1H-imidazole HCl, 1-[β-[3-(4-Methoxyphenyl)propoxy]-4-methoxyphenethyl]-1H-imidazole HCl analogs or salts thereof.

119. The topical lotion of claim 105, wherein the anti-fungal small molecule is N,N,N',N'-*tetrakis*-(2-pyridylmethyl)-ethylenediamine, N,N,N',N'-*tetrakis*-(2-pyridylmethyl)-ethylenediamine analogs or salts thereof.

120. The topical lotion of claim 105, wherein the anti-fungal small molecule is 3,4-Dihydroxy-a-cyanothiocinnamamide a-Cyano-3,4-dihydroxythiocinnamamide, 3,4-Dihydroxy-a-cyanothiocinnamamide a-Cyano-3,4-dihydroxythiocinnamamide analogs or salts thereof.

121. The topical lotion of claim 105, wherein the anti-fungal small molecule is *Discodermia calyx* Calyculin A, *Discodermia calyx* Calyculin A analogs or salts thereof.

122. The topical lotion of claim 105, wherein the anti-fungal small molecule is 3-[1-[3-(Amidinothio)propyl-1H-indol-3-yl]-3-(1-methyl-1H-indol-3-yl)maleimide Bisindolylmaleimide IX Methanesulfonate, 3-[1-[3-(Amidinothio)propyl-1H-indol-3-yl]-3-(1-methyl-1H-indol-3-yl)maleimide Bisindolylmaleimide IX Methanesulfonate analogs or salts thereof.

123. The topical lotion of claim 105, wherein the anti-fungal small molecule is *Nocardiopsis* K252A, *Nocardiopsis* K252A analogs or salts thereof.

124. The topical lotion of claim 105, wherein the anti-fungal small molecule is 1-(5-Iodonapthalene-1-sulfonyl)homopiperazine, 1-(5-Iodonapthalene-1-sulfonyl)homopiperazine analogs or salts thereof.

125. The topical lotion of claim 105, wherein the anti-fungal small molecule is 1-(5-Chloronapthalene-1-sulfonyl)homopiperazine HCl, 1-(5-Chloronapthalene-1-sulfonyl)homopiperazine HCl analogs or salts thereof.

126. The topical lotion of claim 105, wherein the anti-fungal small molecule is (E)3-[(4-Methylphenyl)sulfonyl]-2-propenenitrile, (E)3-[(4-Methylphenyl)sulfonyl]-2-propenenitrile analogs or salts thereof.

127. The topical lotion of claim 105, wherein the anti-fungal small molecule is 3-Hexadecanoyl-5-hydroxymethyl-tetronic Acid, 3-Hexadecanoyl-5-hydroxymethyl-tetronic Acid analogs or salts thereof.

128. The topical lotion of claim 105, wherein the anti-fungal small molecule is *Tabebuia avellanedae* Beta-lapachone, *Tabebuia avellanedae* Beta-lapachone analogs or salts thereof.

129. The topical lotion of claim 105, wherein the anti-fungal small molecule is 2,4-Dichlorobenzamil, 2,4-Dichlorobenzamil analogs or salts thereof.

130. The topical lotion of claim 105, wherein the anti-fungal small molecule is 2-Thioureido-L-norvaline, 2-Thioureido-L-norvaline analogs or salts thereof.

131. The topical lotion of claim 105, wherein the anti-fungal small molecule is 6-Anilino-5,8-quinolinequinone, 6-Anilino-5,8-quinolinequinone analogs or salts thereof.

132. The topical lotion of claim 105, wherein the anti-fungal small molecule is Diphenyleneiodonium Cl, Diphenyleneiodonium Cl analogs or salts thereof.

133. The topical lotion of claim 105, wherein the anti-fungal small molecule is Manumycin A, Manumycin A analogs or salts thereof.

134. The topical lotion of claim 105, wherein the anti-fungal small molecule is Lycorine, Lycorine analogs or salts thereof.

135. The topical lotion of claim 105, wherein the anti-fungal small molecule is 3,5-Diamino-6-chloro-N-[imino(phenylamino)methyl]pyrazinecarboxamide, 3,5-Diamino-6-chloro-N-[imino(phenylamino)methyl]pyrazinecarboxamide analogs or salts thereof.

136. The topical lotion of claim 105, wherein the anti-fungal small molecule is 1,2-Dihydro-3H-naphtho[2,1-b]pyran-3-one, 1,2-Dihydro-3H-naphtho[2,1-b]pyran-3-one analogs or salts thereof.

137. The topical lotion of claim 105, wherein the anti-fungal small molecule is 1-(6-(17β-3-methoxyestra-1,3,5(10)-trien-17-yl)amino)hexyl)-1H-pyrrole-2,5-dione, 1-(6-(17β-3-methoxyestra-1,3,5(10)-trien-17-yl)amino)hexyl)-1H-pyrrole-2,5-dione analogs or salts thereof.

138. The topical lotion of claim 105, wherein the anti-fungal small molecule is 1-(3,6-Dibromocarbazol-9-yl)-3-dimethylaminopropan-2-ol, 1-(3,6-Dibromocarbazol-9-yl)-3-dimethylaminopropan-2-ol analogs or salts thereof.

139. The topical lotion of claim 105, wherein the anti-fungal small molecule is N_1N-dimethylsphingosine, N_1N-dimethylsphingosine analogs or salts thereof.

140. The topical lotion of claim 105, wherein the anti-fungal small molecule is 1-hexadecyl-2-methylglycero-3-phosphatidylcholine, 1-hexadecyl-2-methylglycero-3-phosphatidylcholine analogs or salts thereof.

141. The topical lotion of claim 105, wherein the anti-fungal small molecule is 1-octadecyl-2-methylglycero-3-phosphatidylcholine, 1-octadecyl-2-methylglycero-3-phosphatidylcholine analogs or salts thereof.

142. The topical lotion of claim 105, wherein the anti-fungal small molecule is 3,4-dichloroisocoumarin, 3,4-dichloroisocoumarin analogs or salts thereof.

143. The topical lotion of claim 105, wherein the anti-fungal small molecule is 5,8,11-eicosatriyonic acid, 5,8,11-eicosatriyonic acid analogs or salts thereof.

144. The topical lotion of claim 105, wherein the anti-fungal small molecule is *Streptomyces hygroscopicus* Nigericin, Nigericin analogs or salts thereof.

145. The topical lotion of claim 105, wherein the anti-fungal small molecule is γ,4-Dihydroxy-2-(6-hydroxy-1-heptenyl)-4-cyclopentanecrotonic acidλ-lactone, γ,4-Dihydroxy-2-(6-hydroxy-1-heptenyl)-4-cyclopentanecrotonic acidλ-lactone analogs or salts thereof.

146. The topical lotion of claim 105, wherein the topical lotion is formulated as a cream, an ointment, drops, a gel, a controlled-release patch, a spray, a pessary, or a foam.

147. The topical lotion of claim 105, wherein the topical carrier is selected from the group consisting of mineral oil, sorbitan monostearate, polysorbate 60, cetyl esters wax, cetearyl alcohol, 2-octyldodecanol, benzyl alcohol, liquid petroleum, white petroleum, propylene glycol, polyoxyethylene polyoxypropylene compound, emulsifying wax and water.